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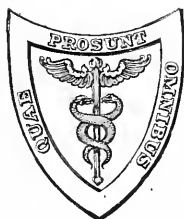
HUMAN INFECTION CARRIERS

THEIR SIGNIFICANCE, RECOGNITION
AND MANAGEMENT

BY

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PREFACE.

THE volume which is herewith presented to the medical public is the outcome of the renewed interest which the subject of Infection Carriers has acquired since the outbreak of the great war, and the resulting necessity of guarding the health of our troops against epidemics. With this has come an evergrowing demand for men trained in the recognition of carriers by laboratory methods and for these, more particularly, the book has been written.

The request from the Surgeon-General's Office that medical students be thoroughly drilled in the epidemiological aspects of the infectious diseases, including the laboratory side of the question, has brought up the problem in what department this training should be given. At the University of Maryland Medical School and College of Physicians and Surgeons of Baltimore, the carrier question was taken up by the Department of Clinical Pathology, to which it would properly seem to belong. The extension of the usual clinical pathological work along these lines has been found most satisfactory from every standpoint. It has already proven of absorbing interest to the student, and will no doubt lead to corresponding work, as a matter of routine, in the clinical laboratories of our hospitals. In the past it has been a source of constant regret to the writer that the clinician and the laboratory worker in so many of our institutions are, for the good of the patient, not sufficiently in touch, and it is for this

reason also, no doubt, that practically no sanitary work of any kind is either demanded or conducted in the majority of the hospital laboratories. It does not speak well for our institutions at which infectious diseases are treated which are apt to result in the development of the carrier state, that previous to the discharge of the patient no examination is made to ascertain whether or not he is apt to prove a menace to others. Team work is here urgently called for between the clinician and the worker in the clinical laboratory on the one hand, and the hospital authorities and the health department officials on the other. The amount of good that would result from such coöperation has been clearly brought out even during the brief period of time that work of this order has been carried on in our military camps, especially when directed by such men as stand at the head of our government sanitary service.

Much of the work and many of the methods which have been collected in this volume are of very recent date. In bringing together the data which seemed of interest and importance, the writer has attempted to be as thorough as possible, but even so, no doubt, many valuable papers may have been overlooked. If this be so, he asks forbearance on the part of his readers and promises to add what may yet be missing in a subsequent edition, if this should be called for.

A general idea of the arrangement of the subject matter may be found from a brief perusal of the table of contents. It will be noted that the book deals with a discussion of the problem under consideration only in connection with those diseases of bacterial origin or which are due to the activity of a filtrable virus in the dissemination of which *healthy human* carriers are now known to play a role, viz., carriers who either have never passed through an attack of the corresponding malady themselves, or, having done so, have

clinically recovered. The maladies in question are cholera, diphtheria, typhoid and paratyphoid fever, dysentery, epidemic meningitis, poliomyelitis, pneumococcus pneumonia, certain streptococcus infections (such as camp septicemia, bronchopneumonia, septic sore-throat, erysipelas and puerperal fever), influenza, and possibly also the pneumonic form of plague.

Under these headings the various phases of the carrier problem have been discussed, *i. e.*, the occurrence of active and passive carriers, the duration of the carrier state, the numerical relation between patients and carriers, the habitat and the virulence of the organisms, the mode of infection, concrete examples illustrating the danger of the carrier to others, the recognition of the carrier with a detailed description of the laboratory methods involved, and the management of the carrier from the standpoint of the public health officer. In conclusion, there have been appended the most important State laws, municipal ordinances, and federal interstate regulations dealing with the carrier problem which have been enacted up to January 1, 1918.

While the book was primarily written for students of medicine, it is hoped that it may prove of some service also to the health officer as well as to the general practitioner, without whose active aid and coöperation any material progress looking to the eradication of infectious diseases from our midst will be impossible.

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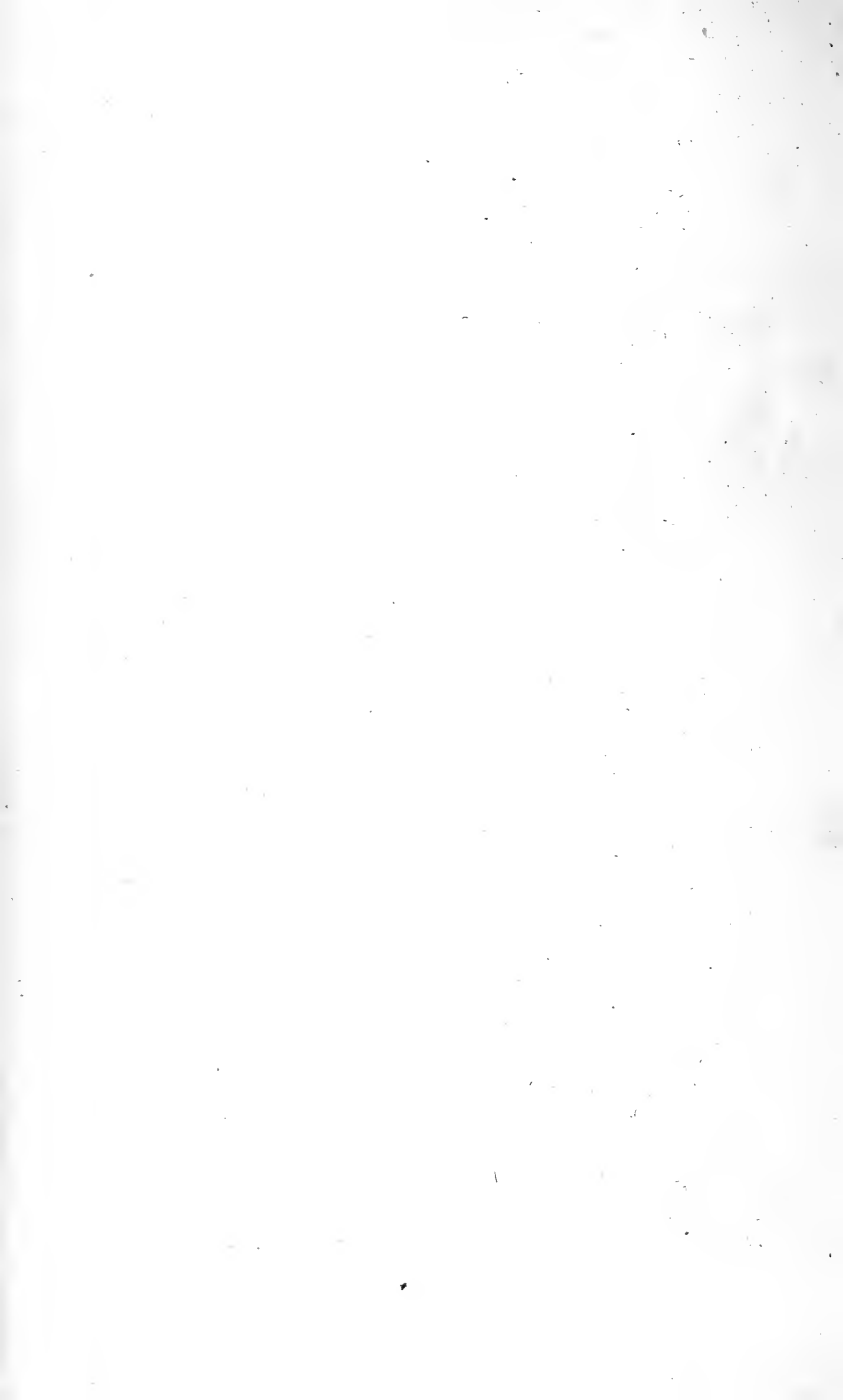
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HUMAN INFECTION CARRIERS.

INTRODUCTION.

THE term "carrier" is used to denote an individual who, while clinically not suffering from the corresponding infection, nevertheless harbors pathogenic organisms in his body, through the elimination of which he is capable either directly or indirectly of infecting others. The discovery that infectious diseases may be disseminated in this manner is of comparatively recent date, and was largely the outcome of the epidemiological study of the cholera epidemic which occurred in certain districts of Germany during the years 1892 to 1894, along lines suggested by Koch. It had, of course, been recognized long before that certain diseases follow the routes of human travel, and that human beings themselves are in some manner concerned in the transmission of the corresponding organisms. But it was assumed that the latter were carried in the individual's belongings, such as his clothing or bedding, and possibly even about the exterior of his own person, such as his hair, his beard, his fingers. Observation has also shown, however, that notwithstanding the most thorough disinfection of every article of baggage that could conceivably have been contaminated, as well as similar treatment of the travelers themselves who were about to leave an infected district, cases of the corresponding disease nevertheless appeared sooner or later beyond the original zone of infection. An investigation of the travelers' past history may have revealed that they themselves had suffered from the disease in question not long before, but they were, to all intents and purposes, perfectly well at the time of their

arrival. In other instances no history of an antecedent illness could be obtained, though the persons may have admitted that they had lived in houses where such illness existed. Still others may have given no history either of a preceding illness or of contact with persons who themselves had been exposed. As, however, no other points of contact frequently existed between the primary and the secondary focus of disease, excepting in the persons of travelers, the question naturally suggested itself whether, after all, these could not have acted as carriers of the corresponding organisms even though they had recovered from the malady or had indeed never been stricken, and as there was no reason for assuming that they carried the organisms about the *exterior* of their persons, there remained the possibility that they might have harbored them in those localities which represent their normal habitat in patients who are actually suffering from the corresponding diseases.

Actual investigation of this question during the cholera epidemic of 1892-1894 showed that this possibility indeed existed; that, on the one hand, persons who had passed through an attack of the malady, no matter how light, might harbor cholera vibrios in their intestinal tract for a variable length of time after recovery, and, on the other hand, that there were perfectly healthy individuals who had at no time shown any evidence of the disease, but in whose feces the organisms could nevertheless be demonstrated. At the time of their discovery these findings, of course, attracted an enormous amount of attention, for the reason that a perfectly simple explanation was here at once afforded of many phases connected with the dissemination of certain epidemic diseases which theretofore had been wrapped in complete obscurity.

Analogous studies were then undertaken in connection with other infectious diseases, and it was soon found that cholera was not the only malady during the convalescence from which the corresponding organisms could persist in the body of the individual, and that perfectly healthy persons could become the carriers of various forms of pathogenic organisms without ever having shown symptoms of the corresponding disease.

It was thus ascertained that convalescents from diphtheria may harbor the offending organisms much longer than the duration of the clinical illness, and represent a very serious menace to the community not only in themselves, but also through the large number of healthy carriers to which they may give rise. The same was then demonstrated for typhoid fever, and with the recognition of the role of the typhoid carrier came the realization that in the dissemination of enteric fever the infected human being is the only essential factor, in the absence of which the disease cannot continue to exist. Then followed the discovery that in the dissemination of meningococcus meningitis also the human carrier plays a most important role; that here also the organism tends to persist after clinical recovery, and that normal human beings may harbor the organism in the upper respiratory tract and cause the infection of others without falling victims themselves to its pathogenic properties. Still more recently it has been shown that poliomyelitis and certain forms of streptococcus infection, as well as certain types of pneumococcus pneumonia, are disseminated in the same manner, and future investigations will no doubt show that still other infectious diseases are transmitted through the activity of carriers of the type that we are here considering.

As I have already pointed out, there are carriers of two kinds. On the one hand there are individuals who have passed through an attack of the corresponding malady themselves, who continue to harbor and excrete the offending organisms after clinical recovery, the so-called *Dauerausscheider* of the Germans; while on the other there are persons who have at no time suffered from the disease—but who have been in contact with patients, or with other carriers, and who like the former are capable of infecting others. Carriers of this latter type the Germans have termed *Bazillenträger*. Practically speaking, it does not appear essential to distinguish between the two, but if for any reason this seems desirable we may appropriately term the first group *active carriers*, meaning thereby that in them the organisms have at one time or another exercised their specific pathogenic activity, while the latter group may

correspondingly be termed *passive carriers*, to denote that in them the organisms have played a purely passive role. But as we shall have occasion to point out in greater detail later on, it does not follow from the existence of the passive carrier state that the individual in question may not fall a victim to the very organisms that he harbors; in other words, that he may not become an active carrier in the sense in which we have suggested the use of this term.

The tremendous influence which the discovery of the existence of carriers must have on our future efforts at control of the corresponding diseases is, of course, apparent at once, and there is scarcely another subject connected with preventive medicine that is deserving of so much attention on the part of the physician and the public at large as this. For this reason it will not be out of place to consider the problem in greater detail in connection with the various diseases in the transmission of which carriers have thus far been shown to play a role. Their sequence has been arranged so as to correspond to the chronological order in which the role of the carrier has been established.

ASIATIC CHOLERA.

THE recognition of the carrier principle in connection with the dissemination of various infectious diseases was first established by Robert Koch¹ in the course of his well-known investigations into the cholera outbreak which occurred in Germany during the winter of 1892-93. In his report to the Government he relates how at the beginning of the Hamburg epidemic, largely in consequence of inadequate assistance, the bacteriological work in connection with the situation was confined practically exclusively to the study of the dejecta of such individuals as were *manifestly* suffering from the disease, or of such as presented clinical symptoms *suggestive* of cholera. It was noted at that time that, notwithstanding the isolation of actual cholera patients and clinical suspects, additional cases appeared nevertheless in the same surroundings. A case in point will illustrate this. On January 8, 2 cholera cases were sent to the hospital, from the Spanish steamer "Murciano," which was tied up at one of the docks. On investigation 4 additional cases were found among the crew, and these also were isolated. The vessel was then moved to another part of the harbor and disinfected. She here lay close to the steamship "Gretchen Bohlen," which had arrived on January 5, and whose crew not only had been free from cholera, but had not even been exposed. The "Murciano" came alongside on January 12 and on the 15th the disease appeared among the crew of the "Gretchen." The inference, of course, was that in spite of the removal of the clinical suspects, and the disinfection of the vessel, members of the latter's crew, even though not ill themselves, must have harbored the corresponding organisms, which no doubt found their way into the water alongside the ship through the flush closets, and were then dipped up by members of the negro crew of the "Gretchen," who used the harbor water not only for washing the decks, but for drinking purposes as well.

On the basis of observations such as this, Koch then insisted upon an extension of the quarantine to contacts, and the bacteriological examination of their dejecta, irrespective of the existence of clinical symptoms and the character of the stools. It was then found that cholera bacilli could occur not only in the dejecta of individuals presenting but slight symptoms of indisposition, but even in those of apparently healthy persons, who had been in contact with cholera patients, to be sure, but who had nevertheless been free and remained free from any clinical evidence of the disease. In other words *they were healthy carriers*. The discovery of such a possibility afforded an immediate explanation of the apparently mysterious manner in which secondary outbreaks of the disease had occurred in different places, where cholera had previously not existed. Outbreaks of this order had been cited as a matter of fact as evidence in favor of the view that Koch's bacillus had in reality nothing to do with the disease, for it was argued, that inasmuch as cholera could be introduced by *perfectly healthy* individuals coming from a cholera focus to a community which had hitherto been free from the disease, the latter could scarcely be caused by the organism in question, the supposition being that the bacillus could not exist in individuals who themselves were not suffering from the malady.

The discovery, however, that this was possible, changed all this and made clear many points which heretofore had been wrapped in complete obscurity. Various important problems now suggested themselves for investigation. It was thus essential to ascertain how long the bacilli could maintain themselves in the intestinal tract after the disease had clinically come to an end; whether or not their virulence remains unimpaired; the frequency of carriers with symptoms so mild as not to suggest the existence of cholera; the frequency of the carrier state in apparently healthy persons and its duration; the habitat of the organisms in the carrier; the manner of transmission of the organisms to others; the relative menace of the carrier as compared with the cholera patient; the question of treatment, etc.

Active Carriers.—As regards the first question, viz., the length of time that the cholera bacilli may persist in the intestinal tract, it appears from the available data that this almost invariably is brief. Guttman² thus reports that in 3 of his 10 cholera convalescents the organisms were demonstrable only to the fifth day, in 2 to the seventh, in 2 to the eighth, and in 2 others to the ninth and in 1 to the tenth day.

Simonds³ found them in every case that came to autopsy up to the sixth day; between the seventh and twelfth in 50 per cent. of the cases; exceptionally only after the twelfth day, and in only one instance as late as the eighteenth day. Rumpel⁴ studied 117 typical cases and could not find the bacilli after the twenty-fourth day; he noted also that in mild cases they disappeared rather earlier than in severe cases, the latest between the eighteenth and the twentieth days. Very painstaking examinations with technically perfect methods have further been recorded by Kolle.⁵ This observer reports that irrespective of the severity of the clinical picture the vibrios in the majority of cases are no longer demonstrable even with the delicate peptone method (see below) between the tenth and the twelfth day. Frequently the cultures were negative already on the seventh or eighth day, and in only 6 of 50 cases did the carrier state extend over the twentieth day. In one single instance, however, the organisms were demonstrable yet on the forty-eighth day. With the exception of a single observation by Dönitz,⁶ in which a positive culture was obtained on the forty-ninth day, the last-mentioned case represents the longest period of time during which cholera vibrios have been demonstrable in the feces of a cholera convalescent.

Corresponding results have been obtained by Lazarus and Pielicke,⁷ Michailow,⁸ Rommelaere,⁹ Abel and Claussen,¹⁰ Greig¹⁴ and others.

As regards the relative number of cholera convalescents who still harbor bacilli after clinical recovery has taken place Greig reports that of 30 patients who had been inmates in the cholera hospital of Puri, India, 11, *i. e.*, 3.6 per cent., were still excreting the corresponding organisms in the stools at the time of their discharge.

Passive Carriers.—While the carrier stage in cholera convalescents is usually quite temporary and only exceptionally extends beyond the second week, and while the quarantine problem in the case of individuals who are known to have passed through an attack of the malady is thus relatively simple, we must not forget that the organisms in question may also be harbored by persons who are apparently in good health, but who have been in contact with cholera patients, and it is this class of individuals that interests us particularly, as they are manifestly a grave menace to others and represent potential foci for the development of outbreaks of the disease in districts in which cholera has previously not existed. As yet but little is known of the relative frequency with which normal individuals may become carriers of this order. As I have already pointed out, nothing at all was known of the possibility of such an occurrence until the German epidemic of 1892–1893 had already passed its climax, and since that time the number of observations that could be made with adequate bacteriological methods was, in Germany at least, relatively small. Pfeiffer¹¹ examined the various members of a family of ten, in which cholera had appeared, and found three carriers of this type. Frosch¹² refers to a study of 42 infected individuals among which 16 were healthy carriers, and emphasizes that of these 12 were children. Friedheim¹³ further reports that of 292 individuals in whose stools cholera vibrios were found 51 were apparently perfectly well. During the minor epidemic which occurred in Germany also, in 1905, and at a time when the importance of examining the stools of all contacts, whether they appeared well or otherwise, was already fully realized, an examination of 212 infected persons revealed the presence of 38 healthy carriers. If then we sum up these data we find that of 561 infected individuals 108, *i. e.*, 19.2 per cent., showed no clinical evidence of disease, or, in other words, that for every 453 actual patients or convalescents, there were 108 individuals who excreted cholera vibrios in their stools without themselves knowing of the danger which they represented to others, and without being suspected, until a bacteriological examination revealed the true state of affairs. While it has been shown that carriers

of this type do not harbor the organisms any longer than individuals who have actually passed through an attack of the disease, that they also are temporary carriers only, they nevertheless represent a most formidable menace to the community as long as the condition lasts.

Virulence of Organisms.—While I have not been able to find any direct statements regarding the virulence of the organisms occurring in healthy carriers, the findings in cholera convalescents may, I think, be properly applied to the former as well, and these have proven conclusively that so long as the organisms can be isolated from the intestinal contents their virulence is practically constant.⁵

Relation of Cholera Carriers to Outbreaks of the Disease.—Koch has repeatedly mentioned that it is frequently impossible to trace an outbreak of cholera to a single individual, even if that individual has himself passed through an attack of the disease. As the organisms may persist in the intestinal tract for as long as seven weeks, it is conceivable that a person may pass through a mild attack in one country without himself realizing the true nature of the ailment, and before the expiration of the carrier stage to arrive at a place thousands of miles away and there to become a primary focus of infection with the rapid development of secondary foci and the resultant outbreak of an epidemic. It is clear that under such conditions the most careful investigation might not reveal the actual source of the outbreak. By the time that the community has come to a realization of the true nature of the disease, the individual in question may indeed have passed the carrier stage and have already left for other parts. This being so, it will readily be understood that it may be even more difficult to trace an outbreak to a passive carrier, *i. e.*, one who has never been ill. But even so, there are a number of instances on record in which the chain of evidence is sufficiently strong as to definitely connect the development of cholera outbreaks with carriers of this order, and to demonstrate what a formidable menace such people represent, so long as they are permitted to remain at large, particularly as they themselves have no knowledge of their condition.

Examples Illustrating the Activity of Carriers.—In this connection an outbreak of the disease in the insane asylum at Nietleben, near Halle, is of special interest.¹ This began in the middle of January, 1893, at a time when the European epidemic was confined to Russia, France, and so far as Germany went, to Hamburg-Altona. During this outbreak 122 cases of the disease developed in the institution. Its origin was investigated with great care. As no persons connected with the institution had come from foreign parts, it is evident that the Hamburg-Altona district was the only one that could enter into consideration as its source. An investigation of the food supply did not furnish any evidence that the disease was introduced in this manner, as the hospitals of the neighboring city of Halle were supplied by the same dealers, and no cases occurred there; and as cases of the disease also developed among individuals who did not receive their board at the institution. A soil origin which in those days was thought to play a role could also be excluded, since the buildings all stood upon a rock foundation. An examination of the sewerage, however, revealed the presence of cholera vibrios and these could also be demonstrated in the water of the river into which the sewerage emptied after passing through the disposal plant. The drinking water was obtained from the same river at a point below the entrance of the supposedly purified sewerage. This water was passed through filters, it is true, but as Koch could show, one of these was evidently in imperfect condition or improperly managed, as the organisms could be demonstrated in the water immediately after its passage through this filter, as well as in a specimen obtained from one of the spigots in the institution.

It was thus clear that with a cholera focus in the institution the organisms would be distributed from this focus through the sewerage and the drinking water supply to the inmates at large. The question then which remained for solution was how that focus developed; in other words, who the individual was who introduced the organisms. As the patients all came from the province of Saxony, and as cholera had not occurred there, this source could be eliminated, unless we assume the very unlikely event that a carrier had travelled from Ham-

burg to Saxony, and had there infected an individual who soon after came to the institution as a patient. More likely is the possibility that the disease was introduced by an employee who was newly engaged. Investigation showed that within the three months preceding the outbreak of the disease thirteen new attendants had been engaged, but that none of these had come *directly* from Hamburg. One individual, however, who came from Halle, admitted that he had lived at the latter place only a few days, and that before that he had been in Hamburg. This same individual had suffered from severe diarrhea on first coming to the institution. While Koch does not regard it as proven by any means that this person originated the epidemic at Nietleben, he merely cites this case as indicating that a connection did undoubtedly exist between Hamburg and Nietleben, and that it is not impossible that one or the other of the newly-engaged employees had after all been in Hamburg, although engaged from Halle, and had possibly purposely neglected to give this information. The evidence, of course, is circumstantial, but as all other sources could be eliminated, it is only logical to conclude that the outbreak was actually due to a carrier, who either had never had the disease, or whose attack had been so mild that he himself was not aware of its true nature.

Another interesting outbreak, which was apparently traced to a definite individual, has been recorded by Greig.¹⁵ During the general epidemic which occurred at Puri in India, in 1912, the disease also appeared in the local jail and led to the development of 17 acute cases, the first occurring on July 27. An immediate investigation revealed that on July 23 a boy aged twelve years had been admitted, who had been attacked by cholera on July 6, and had been a patient in the cholera hospital from that date to July 13, when he was discharged. On July 28, *i. e.*, three weeks after the beginning of his attack, this boy's feces were examined and cholera vibrios found in large numbers. It is noteworthy that the youth had been placed in the "under-trial" ward, and that the disease appeared four days later in this same ward.

While positive evidence regarding the menace which the

carrier represents to all who come in contact with him is, of course, more striking than negative evidence, the latter may at times be of almost equal value. Such evidence is afforded by the fact that although many cholera carriers reached the United States during the past twenty-five years from foreign countries, their recognition and isolation at our quarantine stations have served as a complete safeguard to our country, for not a single instance of the disease has developed during that time on United States soil.

The full extent of the carrier danger we can, of course, only surmise. During the Hamburg epidemic of 1892, 18,000 *recognized* cases of the disease had occurred between August 16 and October 23, leading to 8200 deaths. This represents the primary outbreak of the disease, concerning the origin of which we have no definite knowledge. It may in itself have been due to carrier activity. But, however this may be, we may properly assume that the secondary epidemics which followed the one at Hamburg were certainly, in part at least, referable to such a source. To refer these secondary outbreaks to the distribution of infected clothing and bedding only, would scarcely be warrantable, if we bear in mind the very thorough methods of disinfection which were practiced, and the nature of the quarantine regulations which were then in force. The significance of the carrier, however, it will be recalled, was not yet realized until the primary epidemic had nearly come to an end, and as the period of quarantine against persons coming from the infected district covered only the incubation period of the disease, it will readily be understood that many avenues for the distribution of the malady by carriers really stood wide open. The wonder indeed is that the secondary epidemics were not more extensive. But as the carrier stage is, after all, of relatively brief duration, this factor no doubt, *coupled with the regulations* which were then in force and *which became more rigid as the carrier significance was fully realized*, was sufficient to prevent a wider dissemination of the disease than actually occurred. Subsequently, when adequate bacteriological examinations of the feces of *all contacts* became the rule, which, of course, meant the elimination of the carrier, the disease died out.

Where the carrier goes virtually unchecked, as in India, it is natural that the disease will never die out. An endless chain is here in operation which will not be broken until the carrier problem is solved, and until the frightful danger arising from water pollution by cholera carriers is fully recognized, and appropriate action taken to prevent mass infection through this channel. Hundreds of thousands of people gather here from time to time, coming from all parts of India; they bathe in and drink the holy water of the Ganges, and what wonder that epidemic follows epidemic in the cities in which the people have gathered! The convalescent and healthy carriers then return to their homes, where they give rise to outbreaks of a minor nature, starting new foci, which perpetuate the existence of the organism, and thus furnish the material for larger epidemics, whenever and wherever local conditions favor their development. The religion of the natives is a powerful factor in preventing sanitary progress in that country, but in view of the fact that many of the native rulers have received a European education, and could use their influence with their countrymen, one should imagine that better progress might have been made, and that the responsibility for the continued ravages of the disease may not be attributed solely to *native* conditions.

Mode of Infection.—As regards the manner in which the carrier may disseminate the organisms the same possibilities, of course, suggest themselves as in the case of the cholera patient. As the organisms are present in the intestinal contents, and as infection can only take place through the digestive canal, it is clear that any substance which is capable of serving as a connecting link between the two is capable of conveying the disease. More or less extensive outbreaks will naturally occur and indicate their probable origin by the explosive nature with which they develop, when the drinking water supply of a community becomes infected, and as a matter of fact all major epidemics may be regarded as referable to such a source. Minor outbreaks, on the other hand, may be due to contamination of various articles of food, and isolated cases possibly to a direct transference of fecal material through soiled hands or soiled clothing.

Habitat of Organisms.—While the intestinal contents no doubt represent the most important medium by far, through which the organisms are disseminated, and were long regarded as the only excretion in which they occurred, it appears from the studies of Greig¹⁶ that they may also appear in the urine (urinary carriers). He relates that he was able to isolate the organism from this source in 8 cases out of 55, and that in 2 of these the patients had already recovered and were going about doing their work. In another paper the same writer reports that in one case of cholera¹⁷ he could demonstrate the presence of the comma bacillus in a pneumonic area which implies the possibility of its dissemination through the sputum. These observations are of particular interest as they prove that cholera, like various other bacterial diseases, such as typhoid fever, which were formerly regarded as being essentially local infections, may also be a true septicemia.

Intermittent Elimination.—While the elimination of cholera bacilli in the feces is usually continuous, several investigators have reported that it may also be intermittent. This is important to bear in mind in connection with the question whether a single negative culture may be regarded as evidence that the carrier stage has been passed. Evidently such a position is no longer tenable. Creel¹⁸ reports the case of a sailor on board a transatlantic liner who arrived at New York quarantine with the history of having had an attack of diarrhea and vomiting during the trip. Examination of his feces on August 17 revealed the presence of cholera vibrios. From that date to August 30 all examinations were positive. On August 30 and September 1 negative results were obtained. Between August 30 and September 27, the organism was present on four occasions and absent on six. After September 27 all cultures were negative. Regarding the cause of the intermittency Creel suggests that "gall-bladder infection does not seem likely, as cholera is not a bacteremia, and direct infection from the intestinal canal does not seem probable." He therefore assumed that there were residual masses of fecal material containing vibrios which were not evacuated. Creel, however, evidently was not aware of the fact that several observers had previously found that the cholera vibrio *does* find its way

into the gall-bladder, and that similar conditions thus exist as in typhoid fever, where, as we now know, the gall-bladder is involved in every case and probably represents the sole focus from which the bacilli in fecal carriers at any rate find their way into the intestinal canal. Nicati and Rietsch¹⁹ in 1884 already had reported the presence of cholera vibrios in the bile in 2 cases of the disease out of 3, and on a later occasion in 2 out of 5. Similar findings have been published by Doyen,²⁰ Tizzoni and Cantoni,²¹ Rapschevsky²² and Rekowsky,²³ and still more recently by Kulescha,²⁴ Bruloff,²⁵ Defressine and Cazeneuve,²⁶ Greig²⁷ and Crowell and Johnston.²⁸ Kulescha found cholera vibrios in the gall-bladder in 49 cases out of 109 and definite anatomical lesions in the biliary passages in 10 per cent. of the cases. Bruloff reports the presence of the vibrios in the bile in 76 per cent. of the cases and speaks of their occurrence in the blood and other organs. Greig examined 271 cases and found vibrios in the bile of the gall-bladder in 81, *i. e.*, in practically 30 per cent. In 68 of these no pathological changes were observed in the biliary passages although the comma bacillus was present in pure culture. In others, however, the walls were distinctly diseased. Crowell and Johnston obtained positive cultures from the bile in 65 per cent. of their cases of the actual disease, while of 32 carriers who were detected postmortem the bile was positive in 75 per cent., and it is noteworthy that in 43 per cent. of the carriers the intestinal contents gave a negative result, while the bile was positive.

That the organism reaches the gall-bladder through the blood stream is, of course, the most logical assumption, in view of Greig's findings, as well as those of Bruloff, referred to above, and is further supported by the experiments of Baroni and Ceaparie Victoria.²⁹ These investigators injected cholera vibrios into the ear vein of a rabbit, and found them in the bile thirty minutes later, where they remained demonstrable for one hour after the injection.

Like Creel, Greig¹⁵ also found that the elimination of the vibrios may be intermittent. In 2 of his 11 cases in which the elimination was especially prolonged, there were long intervals—in one instance sixteen days—during which the organisms were not demonstrable.

All these observations are quite analogous to what is known to occur in typhoid fever. The important question, of course, remains whether in those individuals in whom the vibrios persist for a longer time than the average, and particularly in those in whom the elimination is intermittent, infection of the gall-bladder is the responsible factor. To judge from the numerical results obtained by Crowell and Johnston this seems to be the case (see above).

As in the case of typhoid fever it would appear that *the cholera vibrio also cannot maintain itself for any length of time outside of the human body*, and that the elimination of the carrier would therefore lead to the eradication of the disease.

Recognition of Cholera Carriers.—As cholera carriers can only be recognized by adequate laboratory examinations, these are indicated in every individual coming from a focus where cholera is or has been in existence within the period of time that the organisms are known to be able to maintain themselves in the human body, viz., nine weeks. This may, of course, entail an immense amount of labor, but from the results that have been reached it is clear that no other method is applicable, and that the work is hence necessary. At the New York quarantine station 34,000 fecal specimens were examined during the summer of 1911, the necessity for which is apparent from the fact that the cholera vibrio was found in 27 healthy persons, who would have been allowed to pass quarantine with results that can hardly be in doubt, had it not been for the findings in their stools. Corresponding examinations were made at Boston and Providence which were the only other ports having direct Italian immigration. As a result, not a single case of the disease developed in the United States, notwithstanding the constant steamer connection with infected ports in Europe.³⁰ During the same period of time 7338 travellers from suspected ports on the Baltic were examined at Rotterdam and Amsterdam, and 7 cholera carriers found. At Naples 2000 emigrants were examined and 12 carriers discovered. In Egypt an examination of 15,000 persons from suspected ports led to the finding of 22 carriers, and so on. It is clear that the labor is great and will necessitate the coöperation with the usual authori-

ties at critical times of municipal and other laboratories, and the training of the men in these in the laboratory diagnosis of this type of carrier.

Technic.—As regards the technic involved it has been suggested that the individual under examination be given a dose of castor oil previous to the collection of a sample of his feces; with the idea in mind, not only of increasing the number of organisms eliminated, but especially of bringing organisms to elimination during a period of natural intermission. But as this has not proven successful such preparatory treatment may well be omitted. An ordinary specimen only needs to be procured.

The early work in the search for cholera vibrios in the feces was done by smearing gelatin plates from an emulsion of a loopful of the material in question in a few cubic centimeters of bouillon, and allowing growth to proceed at room temperature for about twenty-four hours. Smears were then made from suspicious-looking colonies, which are strongly refracting, yellowish-gray in color and of pin-head size, showing a tendency to liquefy the gelatin, and after staining with the usual dyes examined in reference to the morphology of the organism, which is a vibrio and hence appears as a small curved rod, varying from one to two micra in length.

This method is quite serviceable when the organisms are not present in too small a number, but as the latter is of frequent occurrence, it has been found more advantageous to plant a small amount of fecal material—from 1 to 4 or 5 c.c.—in a flask containing about 250 to 300 c.c. of Dunham's peptone¹ solution which serves as enriching medium, permitting the more rapid development of the cholera vibrios than of the accompanying bacteria. After incubating for six hours at 37° C. a small quantity of the culture is taken from near the surface, transferred to a second flask of the same medium and incubated for about twelve hours longer. If smears from near the surface of this second growth now reveal no vibrios the examination is recorded as negative. If vibrios are found

¹ Dunham's solution contains 10 grams of peptone and 5 grams of salt dissolved in a liter of water by the aid of heat. The solution is filtered and sterilized by the fractional method.

ordinary agar plates are smeared from the peptone solution culture, incubated over night; and suspicious-looking colonies fished the next day, and examined with an anticholera serum of high titer (1 to 10,000 to 1 to 15,000), using a dilution of 1 to 500 and the microscopical test. If the macroscopic method is to be employed, subcultures from the plates are made on agar slants, and these incubated for a period of time sufficient to furnish the necessary amount of material, which is then emulsified and mixed with a suitable quantity of an agglutinating serum, so as to give a dilution of 1 to 500. Controls with normal serum in the same dilution must, of course, also be prepared. A positive result is indicated by the occurrence of instantaneous agglutination, as evidenced by distinct curdling.

If desired, the organism can be further studied bacteriologically and biologically—in reference to its virulence, for example—but for practical purposes the above procedure is sufficient.

Release of Carriers.—A single negative result is, of course, not sufficient to release an individual coming from an infected district from quarantine, as the elimination of the organisms not infrequently is intermittent. To meet this difficulty the only safe procedure would be to hold such persons until repeated examinations covering the period of maximum intermittent latency, viz., twenty-one days (Greig) have shown that the organisms are in reality absent. The quarantine regulations which are actually in force are not as stringent as this and at most, if not all stations, a carrier would be released, if the cultures from the stools gave two negative results at three or four examinations, at intervals of three or four days.

El Tor Carriers.—While the demonstration in the feces of the presence of vibrios, which are agglutinated by a specific antiserum of high titer, in a dilution of 1 to 500, as has been advised above, unquestionably represents sufficient grounds for quarantining the corresponding individual as a carrier, it is well to bear in mind that vibrios have been found in the stools of individuals who have not passed through an attack of the disease, nor have come from a cholera district, which culturally as well as in their behavior toward cholera antiserum cannot be

distinguished from true cholera bacilli. Belonging to this order is the so-called *El Tor vibrio*, so named from its discovery at the El Tor quarantine station among pilgrims returning from Mecca. The organism was found at a time when cholera did not exist either at Mecca, nor among the pilgrims at El Tor. Its true status has given rise to much speculation, and while certain differences exist between it and the cholera vibrio, these differences are of such a nature that they could not be utilized in the study of large numbers of people at quarantine stations, let alone in places where cholera is actually existent. From a practical standpoint these El Tor carriers should be treated exactly as the cholera carriers, *i. e.*, they should be quarantined until the organisms have disappeared from the feces.

Aside from the El Tor vibrio, other vibrios have been described as occurring in the stools of cholera convalescents and contacts and at times alternating with the true cholera vibrios, but differing from these in the fact that they are not agglutinated by anticholera serum of high titer while they may be agglutinated by the person's own serum.^{15 28} The status of these organisms also is as yet an open one, but inasmuch as they have thus far been observed in cholera convalescents and contacts only, it may be just as well to extend the quarantine period of such individuals until these organisms also have disappeared.

In conclusion I would briefly refer to the suggestion that in place of the fecal examination a *serological examination of all cholera suspects* be made and that the former be resorted to only when the latter shows that an individual's serum gives an agglutinative reaction with a standard strain of the cholera vibrio. It has been shown as a matter of fact that the blood serum of cholera carriers does contain agglutinins. Greig¹⁵ thus mentions that even in the 2 carriers with long periods of intermittency (sixteen to twenty-one days), which he had occasion to study with special care, agglutination was obtained, while all the others who did not show the comma bacillus in their stools gave a negative result. Analogous results have been reported by Massaglia.³¹ As yet our information on this point is too meager, however, to warrant the

substitution of the serological for the direct bacteriological method. In order to come to a conclusion the two examinations should be made side by side in a large series of cases, and for this work we no doubt will have to look to our colleagues in the East. Meanwhile the bacteriological examination of the feces should be relied upon at the various quarantine stations.

Management of Cholera Carriers.—*Quarantine.*—As it is absolutely essential that no cholera carrier should be permitted to be at large, it follows that at times of epidemics no convalescent should be discharged from observation until repeated examinations of his feces have proven that he no longer harbors the organisms, and that every contact be quarantined and examined in the same manner. Bearing in mind the occurrence of intermissions in the elimination of the organism it would further seem indicated that the quarantine be maintained until repeated examinations over a period of three weeks have shown only negative results, unless indeed the individual has actually been removed from the focus of infection for a period of seven weeks, in which case a single negative examination would suffice to warrant his release. In other words, so far as quarantine is concerned the carrier should be treated exactly as a case of the actual disease. Upon his release he should be kept under surveillance for a reasonable length of time, and in the event of his wishing to change his place of abode to another town the authorities at that place should be notified of his coming and the individual be ordered to report himself immediately upon his arrival. These regulations are actually in force in our country, and coupled with adequate laboratory control have furnished complete protection.

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DIPHTHERIA.

Active Carriers.—Following the announcement by Escherich¹ in 1890 that he had found diphtheria bacilli in the throats of convalescents from the corresponding disease, during the first three days after the disappearance of the membrane, the question naturally arose for how long a time such individuals could remain a menace to others. This problem has been widely investigated and the conclusion reached that the organisms may not only persist for a number of days following clinical recovery, but for weeks and months and even for years; in other words, that the diphtheria patient may become a carrier of variable duration. One of the most extensive investigations in this direction was conducted by the Health Department of New York City in 1893-1894, under the direction of Biggs, with the assistance of Park and Beebe.² An analysis of 752 cases, which were studied with reference to the length of time that the organisms may remain in the throat, showed the following: In 325 cases, *i. e.*, in 43.2 per cent., the bacilli disappeared within three days after the complete disappearance of the exudate; in 427 cases, *i. e.*, in 56.8 per cent., they persisted for a longer time, *viz.*:

In 201	<i>i. e.</i> 26.7	per cent.	for 5 to 7 days	
84	<i>i. e.</i> 11.1	"	"	12 "
69	<i>i. e.</i> 9.1	"	"	15 "
57	<i>i. e.</i> 7.5	"	"	3 weeks
11	<i>i. e.</i> 1.4	"	"	4 "
5	<i>i. e.</i> 0.6	"	"	5 "

Another large series of cases was investigated during 1900 by Prip.³ The organisms could here be demonstrated in 345 out of 654 cases, *i. e.*, in 52.7 per cent., while the membrane persisted in the fauces; whereas in the remaining 309

cases, *i. e.*, in 47.3 per cent., they were present for a longer period of time, *viz.*:

In 118	<i>i. e.</i> 18.0	per cent. for	1 to	10 days
93	<i>i. e.</i> 14.8	"	"	10 to 20 "
51	<i>i. e.</i> 7.7	"	"	20 to 30 "
41	<i>i. e.</i> 6.2	"	"	30 to 60 "
4	<i>i. e.</i> 0.6	"	"	60 to 90 "
2	<i>i. e.</i> 0.3	"	"	90 to 120 "

Tjaden⁴ has reported examinations in 1338 cases, which were carried on until the bacilli had disappeared, with the following results:

In 897 cases,	<i>i. e.</i> 67.0	per cent. the organisms were gone after	2 weeks
1004 "	<i>i. e.</i> 75.0	"	" 3 "
1109 "	<i>i. e.</i> 83.6	"	" 4 "
1192 "	<i>i. e.</i> 89.1	"	" 5 "
1248 "	<i>i. e.</i> 93.4	"	" 6 "
1297 "	<i>i. e.</i> 96.9	"	" 7 "
1303 "	<i>i. e.</i> 97.4	"	" 8 "
1329 "	<i>i. e.</i> 99.3	"	" 9 "
1331 "	<i>i. e.</i> 99.5	"	" 10 "
1336 "	<i>i. e.</i> 99.9	"	" 11 "
1337 "	<i>i. e.</i> 99.95	"	" 14 "
1338 "	<i>i. e.</i> 100.0	"	" 17 "

Similar findings have been published by Glücksmann,⁵ Scheller,⁶ M. Neisser and Heymann,⁷ E. Neisser and Gabriel,⁸ and many others. From the collected data we may conclude that approximately 85 per cent. of diphtheria convalescents are free from bacilli by the end of the fifth week, and 98 per cent. by the end of the ninth week; or, in other words, that 15 per cent. of the cases harbor the organism even after the fifth week and 2 per cent. after the ninth week. But there is evidence to show also that exceptionally the bacilli may persist in the throat (or nose or both) for a much longer time. Hewlett and Nolan⁹ have thus reported a case in which they were found after six months. Fibiger¹⁰ demonstrated them in one case after nine months and Le Gendre and Pochon¹¹ after eighteen months. Prip³ mentions a case in which they were found after four years, and Neisser has described an instance of chronic nasal diphtheria in which he could isolate the organisms after eight years.

There is thus abundant evidence to show that the diphtheria patient may become a diphtheria carrier, and while in the majority of cases this condition is of relatively brief duration, it may last sufficiently long, in a not inconsiderable percentage of cases, as to warrant the classification of such individuals as *chronic* carriers. The significance of this discovery will become apparent at once, if we apply the figures given above to conditions as they actually exist in any one of our large cities at the present time. During the twelve months ending November 30, 1915, there occurred in greater New York 15,402 cases of diphtheria. On a minimum basis of 15 per cent. it would follow that 2310 cases were thus in the carrier stage for a period exceeding five weeks. I say "a minimum" advisedly, for this figure does not include those cases in whom the carrier stage persists for a longer time than twelve months, nor those who have become carriers without ever having suffered from the disease.

Passive Carriers.—That the latter occurrence is possible, and indeed very common, is now well known. Loeffler¹² in his first publication had already mentioned the fact that in the course of an examination of twenty children he found bacilli which were morphologically and biologically indistinguishable from true diphtheria bacilli in the throat of a child, notwithstanding the fact that this one had never suffered from the disease and was, to all intents and purposes, perfectly well at the time. This observation was for some time indeed referred to by his opponents as evidence against the etiological relationship of the organism to the disease in question. Subsequent investigations showed, however, that such an occurrence is by no means rare, and that the organisms in question are actually diphtheria bacilli, presenting all the characteristics of those that may be isolated from actual cases of the disease. The majority of cases of this order are represented by persons who have been in contact with diphtheria patients. In a series of forty-eight children who had been in more or less intimate contact with the disease, Park thus found bacilli in 50 per cent., though it is to be noted that conditions in these particular families were the best possible for the transmission of the bacilli from one

to the other. But even in families where the isolation of the patient had been satisfactorily carried out, the organisms were found in a fair number of the other children. Park mentions that this was the case in less than 10 per cent., but even so it will be realized that on an 8 per cent. basis, and allowing three children to a family (two well to one actually sick), and applying the 15 per cent. carrier basis to the resulting number, our actual number of carriers would be increased by 369, giving a total of 2679. But even this number, conservative as it is, is as yet too low, for there still remain to be added those carriers who have not developed from any known contact with actual cases but from other carriers. Regarding the frequency of such cases, Park also has furnished us with definite information: Of 280 children in New York who gave no history of direct contact with diphtheria, eight were found to harbor true virulent diphtheria bacilli in their throats, which would correspond to 2.8 per cent. This, calculated for the entire child population of Greater New York, would give us truly a most formidable number to which there would still have to be added a not inconsiderable number of adult carriers, who have neither had the disease themselves nor been in contact with cases of the disease. Park, himself, concludes from his studies that virulent diphtheria bacilli are present in probably about 1 per cent. of all healthy throats in New York City! This figure agrees very closely with the findings of Goldberger, Williams and Hachtel³² who found thirty-eight carriers in the course of an examination of 4093 healthy individuals, which gives a percentage of 0.9.

The conclusions reached by Park have been confirmed by practically all observers who have had the opportunity to investigate large series of suspects. Vogt¹³ and Johannesen¹⁴ each found diphtheria bacilli in 3 out of 26 apparently healthy children; E. Müller¹⁵ in 24 out of 100. Stenmeyer¹⁶ reports that in the course of his investigations in Rotterdam he found 7 per cent. of the people harboring diphtheria bacilli in the absence of any corresponding lesion. Kober¹⁷ examined 600 healthy school-children and found virulent diphtheria bacilli in only 5, and avirulent organisms in 10. Scheller⁶ states

that in his large series of examinations positive findings were recorded in 38 per cent. of the healthy entourage of diphtheria patients, and he adds that he regards even this figure as too low, since it is based on single examinations only. Sommerfeld¹⁸ found bacilli in 8 children out of 368 in a general hospital, viz., 2.1 per cent., while Beck¹⁹ and Fibiger,²⁰ on the other hand, failed to find diphtheria bacilli in 66 and 82 healthy individuals, respectively, in whom contact with diphtheria could be definitely excluded. As a matter of fact there is sufficient evidence to warrant the conclusion, that among people who have never, not even remotely, been in contact with actual cases of the disease, diphtheria carriers are very rare, and that there is nothing tangible to support the view that the organism is more or less ubiquitous, as was formerly believed.

Regarding the frequency of diphtheria carriers among the entourage of diphtheria patients in military life, Labit³³ mentions that in his experience the average was 28.9 per cent., and that frequently the 50 per cent. mark was reached. He relates that on one occasion a single case of the disease gave rise to nineteen carriers among the nurses and attendants, and that these in turn produced others in such numbers that it became necessary to isolate the physically fit of the entire unit and to give them employment as gardeners and the like. McCord, Friedländer and Walker,³⁴ on the other hand, who conducted their investigations at Camp Sherman, found that of 3215 exposed persons only 2.76 per cent. were what they term contact, viz., passive carriers. Such wide differences can, of course, be explained in part on the basis of the much more favorable conditions under which our national army recruits lived during their period of training in this country, as compared with those which must exist among actual fighting units. But even so, remembering the overcrowded condition of the camps and base hospitals, during the past winter, it is surprising that such a low carrier incidence should have existed. The observers last mentioned remark that, if corresponding figures should be obtained at other camps, it is permissible to maintain that diphtheria is not a major camp disease,

and that the occurrence of sporadic cases is not a matter of special gravity. With this view other observers do not agree. Keefer, Friedberg and Aronson,³⁶ while stationed at Camp Doniphan, thus report that "during the early months of 1918 the control of diphtheria, with special reference to the carriers of the disease, was a very serious problem which for a long time seemed but little influenced by the strenuous efforts of the staff." During a period of four months 461 cases of clinical diphtheria and 686 carriers were observed. "Even at a time when but few cases of the actual disease were under treatment more than half of the twenty-six wards of the hospital contained carriers among patients and attendants. And although cultures were made of all in such wards and infected individuals removed, the next search, at an interval of from five to seven days, was sure to reveal at least as many more who harbored the organism."

Habitat of Organism.—As in the case of various other pathogenic organisms there is steadily increasing evidence to show that the normal and exclusive habitat of the diphtheria bacillus is the diphtheria patient and the diphtheria carrier. In both, moreover, it is exclusively the mucous membrane of the nose, the throat and the mouth, with the communicating structures, which enter into consideration.

In the great majority of cases the carriers harbor the bacilli in the tonsils. In a small number the organisms are found only in the nose and in the most persistent carriers of this type chronic inflammatory or atrophic processes are almost invariably demonstrable.³⁶

The middle ear is apparently infected in many cases of the disease and it is noteworthy that this frequently occurs at a time when the patient has, apparently, already entered upon the stage of convalescence. Wolff²¹ mentions that in nasal diphtheria the corresponding sinuses are always involved. In one case of this order he could demonstrate diphtheria bacilli in the nose on the one hundred and twenty-first day following the beginning of the disease. Those relatively rare cases in which the disease attacks the skin, the genitalia and the stomach hardly enter into consideration from the standpoint of the carrier.

Virulence of Organisms.—That the bacilli in the throats of carriers may be virulent has been abundantly demonstrated not only by the animal experiment, but also by the relative frequency with which healthy child carriers fall victims to their own organisms. Of the 50 per cent. in which Park thus found diphtheria bacilli among those children in whose families actual cases of the disease had occurred, 40 per cent. later developed corresponding lesions, and of the 8 positive cases among the 280 healthy children without a history of contact, two developed diphtheria some days after making the cultures. From these observations it follows also that the existence of the carrier state in a healthy person does not necessarily indicate that the individual is immune.

Non-virulent Strains.—One factor which has complicated the elucidation of the true state of affairs in connection with the diphtheria carrier problem is the not infrequent occurrence in the throats of perfectly healthy individuals of non-virulent diphtheria bacilli, on the one hand, and pseudodiphtheria bacilli, on the other. So far as the above figures are concerned these have reference exclusively to the presence of virulent organisms, and it is extremely gratifying that Park has paid such careful attention to this very point. That the organisms harbored by carriers are not necessarily virulent, however, is now also known. Goldberger and his collaborators thus found that of nineteen carriers only two harbored bacilli of high virulence.³² The non-virulent organisms differ in no wise from the virulent variety, except in the animal experiment, and like the virulent type they produce acid in bouillon. Just what their significance is we do not know, but manifestly they are not of moment so long as their lack of virulence lasts.

Pseudodiphtheria Bacilli.—So far as the differentiation of the pseudodiphtheria bacilli from the true organisms is concerned, mistakes are particularly apt to happen if the observer is not thoroughly familiar with the normal variations in the morphology of both types. Fortunately, it is more common that pseudoorganisms are mistaken for the true variety, than the opposite. Scheller,⁶ whose experience is probably typical of that of most investigators, remarks

that with increasing experience he saw pseudobacilli less and less frequently, and that in his last series of 1500 examinations he did not meet with them in a single instance. (See below.)

Mode of Infection.—Considering the extraordinary number of carriers, it is, on first consideration, surprising that diphtheria is not more prevalent than is actually the case; but we must remember that mere contact with a carrier is not sufficient to cause the disease. To bring this about the contact must be intimate, the dose sufficiently large and the recipient susceptible. Unless these three conditions exist, infection will not occur. As the mucous membrane of the upper respiratory tract with its communicating structures represents the habitat of the diphtheria bacilli in the carrier, as well as in the patient, the organisms are doubtless conveyed to others in the salivary “spray” during conversation at close range, through the act of sneezing and coughing, through the common use of eating and drinking utensils, through toys, etc.

The best protection against infection is, without doubt, an intact healthy mucosa. When this barrier is broken, be this in consequence of a local inflammatory condition or of an injury, the road is open for infection, and under such conditions the carrier may fall a victim to his own organisms, which he may have “carried” for a long period of time without injury to himself. But even though the chances of infection through the carrier are relatively less than through contact with diphtheria patients, the carrier nevertheless represents a very real and, at times, most formidable menace to the community, for to the *manifest* danger from the patient is added the unknown element of the *hidden* foe. Against the former a defence is possible, for the very reason that the danger is manifest, while against the individual who himself is usually unaware of his fatal gift, the public is not on guard. Unfortunately, we have no actual figures to show just what percentage of diphtheria cases are due to carriers, but that this percentage may be quite high is evident from the histories of certain outbreaks which have actually been traced to such a source. A few histories of this order are here related:

Examples of Infection by Carriers.—A young married woman while living in H. was taken ill with diphtheria. After recovering, she visited her family in the small fishing village B. where no diphtheria case had occurred within recent years. About a fortnight later a younger sister, living in the same house, developed the disease; then another member of the family, then still another, and yet another, until of the entire household of about a dozen people, all, with the exception of two, had been stricken. From this focus the infection then rapidly spread from farm to farm, and from hamlet to hamlet, until the total number of cases numbered approximately a hundred, with an appalling rate of mortality, in the absence of practically any treatment. While no cultures were taken there can be no reasonable doubt that the young woman in question was a carrier at the time of her return to her family.

A very interesting epidemic of diphtheria occurred at the Johns Hopkins Hospital and Medical School in 1911, which could be explained only on the basis of the activity of a carrier.²² On January 25 a pupil nurse was admitted with the disease to the isolation ward. On February 3 a patient in the male medical ward F was stricken with the malady. On February 9 a pupil nurse in charge of the children in ward G developed diphtheria, and, on the following day, an employee in the baggage room was taken ill. On February 11 there followed a case in a child in ward G; on February 13, 2 more cases developed in children in the same ward and on February 15 a fourth-year student doing service in the same ward was found infected; 8 cases had thus developed within a period of twenty-two days, and 5 of these in the same ward. Up to this time the situation was not regarded as out of the ordinary. "A more or less systematic examination" of patients, nurses and students in ward G was carried out at this time, but no additional cases were brought to light. On February 20, however, another fourth-year student serving in the same ward was found infected, and on February 21 3 adult patients and 3 nurses, likewise from ward G, also another nurse, a roommate of one from the infected ward, as well as a nurse in the general operating room who had

handled ward G patients. On February 21 a systematic examination of the hospital population was then begun and "on the slightest appearance of suspicious symptoms the individuals were segregated and cultures taken." On February 22, 3 additional cases were discovered, an adult patient, a nurse in ward G and a medical intern in another ward. On February 23, 7 more cases were found, viz., two more children in ward G, three nurses and a member of the second-year medical class. On February 24 there followed 11 cases, viz., two more nurses, a patient in ward F and eight medical students. To date 38 cases had thus developed within a month, and it was evident that the disease was rapidly spreading from its chief focus in ward G. On February 25 the medical school was ordered closed. On February 26, 6 additional cases developed and on February 27, 8 more, of which 3 occurred in members of the Faculty or their families, making a total of 52 cases. The dispensary was then closed, so as to admit no more patients to the hospital, with the exception of urgent cases. The medical school buildings and the students' dining room were disinfected and 300 persons injected with a prophylactic dose of diphtheria antitoxin, viz., 200 nurses, 43 students and a small proportion of the resident staff, as well as various patients. Hereafter the epidemic gradually subsided, although 20 additional cases occurred between February 27 and March 22, when the epidemic definitely came to an end.

It is difficult to account for the development of an epidemic, such as the one just described, on any other basis than that of the carrier, but unfortunately routine bacteriological examinations were not undertaken until the epidemic had already made considerable headway, so that the original path of infection could no longer be traced. This same objection to a lack of an *ad oculos* demonstration of the primary carrier applies to most outbreaks of this order. But we must bear in mind that with a type of infection like diphtheria, in which transmission occurs not through a food or water route, as in typhoid fever, but through the air, the tracing of the *original* carrier must of necessity be very difficult, though the discovery of the secondary carriers

should be a simple matter if routine cultures are made as soon as the first case of the disease appears. Mere throat inspection is manifestly not sufficient.

The direct connection between a carrier and an outbreak of the disease has, however, been satisfactorily demonstrated in a number of other cases. Hellstroem²³ thus relates the following instance: Between December 12, 1894, and February, 1895, 25 members of a certain regiment stationed at Stockholm were taken ill with diphtheria. As it was thought that the outbreak was possibly due to some latent, abortive cases or to carriers, Hellstroem made cultures from 15 members of the same regiment, whose throats appeared reddened, but who showed no signs of the disease. In 3 of these diphtheria bacilli were found. At this time a servant girl was brought to the hospital for contagious diseases, suffering from a severe case of diphtheria. Regarding the origin of her infection nothing could at first be learned; no diphtheria cases had occurred at her place of service, nor among her relatives or friends. It was found, however, that she was engaged to a sergeant of the regiment in question, and on examination diphtheria bacilli in abundance could be cultured from the man's throat, in spite of the fact that physical examination revealed no evidence of disease. Thereupon the entire regiment was cultured and diphtheria bacilli discovered in 19.21 per cent. of the men, in the absence of any exudation. All carriers were now isolated and the quarantine suspended only after the bacilli had disappeared. Three to four weeks following the establishment of quarantine, a young girl was admitted to the hospital suffering from diphtheria. It was learned that she was the daughter of one of the isolated men, and that the latter had visited his home contrary to orders. Hereafter the carriers were all transferred to the hospital until they became bacillus-free, after which no more cases developed in the regiment.

Another instructive example of carrier activity has been recorded by Fibiger:¹⁰ In this instance an outbreak of 8 cases had occurred in a certain school. Fibiger examined 134 individuals who had been in direct or indirect contact with these cases and discovered bacilli in 8. Whereas imme-

diate isolation of the *patients*, besides a general and repeated disinfection had not arrested the outbreak, this stopped as soon as the *carriers* had been quarantined and thereafter not a single case developed within eighteen months.

Recognition of Diphtheria Carriers.—The recognition of the diphtheria carrier is possible only on the basis of a bacteriological examination of the throat and nose, and it is well to bear in mind that the presence or absence of any redness of the throat is of little moment either as evidence pro or contra. Unless this be remembered much valuable time will be lost in combating an outbreak of the disease. When a case of diphtheria develops in a private household every member of that household should be promptly cultured. When a case develops in a school or an institution, or a factory; in short, within a local community, cultures should be taken of every individual with whom the patient could possibly have come into contact. If any mistake should be made it should be in the direction of too extensive an investigation rather than the reverse. Then and only then is there a reasonable chance of preventing the malady from spreading. Where this is not done a more or less extensive epidemic will be the almost inevitable consequence. It is for this reason that the occurrence of a case of diphtheria in a country district is so much more serious than in a city. In the country a bacteriological supervision is practically out of the question, and in a very short time a vicious circle between carriers and patients becomes established, which only too often is not broken until there is no further susceptible human material available for the propagation of the disease. While an examination of the throat and nose is thus a *sine qua non*, it is well to remember the frequency with which a median otitis develops in connection with diphtheria, and to include an examination of any ear discharge in the general investigation.

The *standard culture medium* is Loeffler's blood serum. Tubes or plates of this should be streaked with sterile swabs on which some of the secretion from the pharyngo-tonsillar region, on the one hand, and the posterior nares, on the other, has been collected. When swabbing the throat special pains should be taken, if at all possible, to obtain secretion from the

tonsillar crypts (particularly the anterior one), as it is here that the organisms are most apt to persist in carriers. To this end *it is advisable to use small swabs* rather than large ones and to penetrate into the crypts as deeply as possible.

In our larger cities which can boast of a bacteriological laboratory in connection with the health department, suitable outfits for cultural purposes are readily obtainable and sanitary inspectors are available for work which the general physician will not or cannot undertake. In country districts, however, the community practically stands defenseless before this most formidable disease, and it is urgently necessary that steps be taken by our legislative bodies to furnish adequate protection in this direction through the establishment of rural laboratory stations provided with an adequate and properly trained personnel.

While it is exceptionally possible, in *carriers*, to find diphtheria bacilli in the smear made directly from the swab, no reliance should be placed upon such technic. Culture should be resorted to in every case. A positive result *may* already be reached at the expiration of six to eight hours' incubation, but it is wiser to wait a longer time, as some of the characteristic features of the organism frequently only develop after an incubation extending over eleven to thirteen hours. At the expiration of this time smears are then prepared and stained with a suitable mixture such as that suggested by Neisser, particularly one made up according to the following formula. This calls for three solutions: The first contains 1 gram of methylene blue dissolved in 20 c.c. of alcohol, to which 50 c.c. of glacial acetic acid and distilled water are added to the 1000 c.c. mark. The second is made by dissolving 1 gram of crystal violet (Höchst) in 10 c.c. of alcohol and diluting with distilled water to 300 c.c. The third solution is prepared by dissolving 1 gram of chrysoidin in 300 c.c. of hot distilled water and filtering. The smears are stained with a mixture of two parts of number one and one of number two for ten to fifteen seconds, after which they are washed in water, and counterstained for an equal length of time with number three. This mixture brings out in a perfect manner not only the polar bodies, but the morphology of the bacilli as well,

and for purposes of diagnosis it is essential that both be shown, and above all, that the observer be thoroughly familiar with the latter, more particularly. If the duration of the incubation be as indicated this method alone is perfectly sufficient for the diagnosis. Loeffler's solution need then not be employed. If, however, the cultures are to be examined after five or six hours, already the latter will be found of advantage. With the use of Neisser's solution the differentiation of the true from the so-called pseudodiphtheria bacilli or similar organisms will cause the experienced worker no difficulty, and it may be well to emphasize that the pseudoorganisms are after all rarely met with and show no granules, if the above technic is employed. As Scheller remarks in commenting on this point, he saw fewer and fewer organisms which he diagnosed as pseudobacilli as his experience grew, and in his last series of 1500 examinations he did not encounter them even once. When in doubt it is best to transplant the suspicious colonies, and it will then be found that the second generation will show the typical structure, if they are indeed true diphtheria bacilli. In conclusion it is the better and safer course to call doubtful looking organisms diphtheria bacilli than to view them as harmless pseudobacilli.

Virulence Tests.—Whether the organisms that have been diagnosed as diphtheria bacilli on cultural and morphological grounds are virulent or not is another question which cannot be decided without resorting to the animal experiment. For practical purposes it will be best to regard all such organisms as virulent, and to act upon this basis, unless there be special reasons to the contrary. If the animal test is to be made it is advisable to follow the advice of Behring, Escherich, Koplik and others, viz., to use young guinea-pigs only—weighing from 350 to 450 grams. These are injected subcutaneously with 0.25 to 0.5 per cent., and in special cases even with 1 per cent. of their body weight of a forty-eight-hour-old culture in bouillon. If the organisms are virulent the animal may show evidence of serious illness after six to eight hours, and death usually occurs within thirty-six to seventy-two hours. Especially characteristic at autopsy is a marked congestion of both suprarenals.

To economize animal material the method of Zingher and Soletsky³⁷ may also be employed. To this end a colony is fished, smeared over a tube of blood serum, and this incubated for twenty-four hours, when the growth is washed off with sterile saline, a fairly dense emulsion being prepared. Of this 0.1 to 0.2 c.c. is injected intracutaneously into a guinea-pig. If the organism was virulent an area of redness and induration develops in from twenty-four to forty-eight hours, which usually proceeds to necrosis.

The Management of the Diphtheria Carrier.—*Quarantine.*—The *sine qua non* in connection with any measures aiming at the eradication of diphtheria is, of course, the isolation of the patient and of those who have to do with his care until as least two consecutive bacteriological examinations with an interval of twenty-four hours of both throat and nose have shown that they are free from the corresponding bacilli. So long as no adequate provision exists in our cities for the compulsory removal of diphtheria patients of the humbler walks of life to suitable hospitals, so long will diphtheria remain with us and so long as physicians disregard the law which calls for the notification of the department of health of every case of diphtheria, so long will the health and lives of others be menaced. Much headway has been made, to be sure, in the attempt to eradicate the disease from our midst, and fairly satisfactory laws and regulations to this end have been enacted in many of our States and cities. (See Appendix.) That these regulations, however, are in part insufficient, and in part insufficiently observed is evidenced by the fact that diphtheria even in our large cities is yet a very common malady; and were it not for the fact that we have learned to control its severity by the timely use of antitoxin, it would still rank high among our most formidable diseases.

We have seen that while a large percentage of diphtheria patients become carriers during their convalescence, the duration of the carrier stage is relatively short, so that no great hardship will result from the necessary isolation; and what is true of the diphtheria convalescent is true of the entourage of the patient in which the carrier condition may have developed. Quarantine for both is absolutely necessary and should

not be lifted until at least two successive bacteriological examinations of both throat and nose, separated by an interval of twenty-four hours, have given a negative result.

Use of Masks.—Particularly important as a preventive method both in reference to the direct dissemination of the disease by patients as well as the production of carriers, is the use of gauze masks,³⁵ both on the part of the patient himself and his attendants. This cannot be insisted upon too strongly. Its value has been thoroughly established in the base hospitals connected with our military camps, and it is high time that the health authorities and the medical profession of civil communities also should recognize its importance and insist upon its use in the management not only of diphtheria cases, but of all maladies which are disseminated through the secretions of the respiratory tract.

Medical Treatment of Carriers.—A good deal has been written regarding the question whether or not it is possible to shorten the carrier stage, and especially whether or not it is possible to cure the condition in the chronic cases, by medicinal or other methods. *A priori* one should expect this to be possible, bearing in mind that the organism is not a very hardy one, and most observers are agreed that the local application of various disinfectants is of distinct benefit. Park² thus pointed out that in one-half to two-thirds of the cases thorough irrigation of the throat and nose with a 1:4000 bichloride of mercury solution, at intervals of a few hours, will lead to the disappearance of the diphtheria bacilli within three or four days following the disappearance of the membrane. But in the remainder they persisted nevertheless. Loeffler¹² recommended his well-known mixture, composed of 36 c.c. of toluol, 60 c.c. of absolute alcohol and 4 c.c. of liquor ferri sesquichlorati, to which 10 grams of menthol were added to lessen the pain attending the application of the remedy. This mixture, as a matter of fact, is very efficacious when it can be brought into intimate contact with the organisms, but unfortunately this is possible only to a limited extent. The same is true of the local application of many other substances, such as hydrochloric acid and various chlorides, as zinc chloride, the double chloride of sodium and gold, the tri-

chloride of iodine; further of nitrate of silver, collargol, lactic acid, potassium chlorate, sulphurous acid, hydrogen peroxide, etc. Wassermann²⁴ recommended the local application of a bactericidal serum, prepared by injecting animals with the dead bodies of bacilli, but this also does not appear to lead to the desired end. Emmerich²⁵ recommended a ferment obtained from the *Bacillus pyocyaneus*, which in the test-tube brings about the digestion of the bacilli, and which is said to be of great benefit in the treatment of pharyngeal diphtheria, with extension into the larynx and nose; but there is thus far no satisfactory evidence that the carrier stage can be satisfactorily influenced in this manner. More recently it has been suggested that the diphtheria bacilli can be crowded out by the introduction of pure cultures of the *Staphylococcus aureus*. This idea is based upon the observation of Schitz²⁶ that the bacilli disappeared in some cases following a supervening infection with staphylococci. While several investigators²⁷ have reported encouraging results, others did not find that the period of quarantine was appreciably lessened by this method.²⁸

Inhalation of various disinfectants has also been suggested, but so far as the results go that have been recorded in the literature, no very satisfactory conclusions can be drawn. In the French army the following procedure was in vogue in 1910: A mixture composed of 12 grams of iodine, 2 grams of guaiacol, 25 grams of thymol and 6 grams of potassium iodide, dissolved in 200 c.c. of 60 per cent. alcohol, was poured into a porcelain dish, and this floated on a basin of boiling water. The carrier was then instructed to inhale the fumes from this mixture at five sittings of two or three minutes' duration in the course of twenty-four hours. As no report has appeared concerning the efficacy of this treatment we may assume that it was not very successful.

Petruschky²⁹ and others have used a vaccine made of dead diphtheria bacilli, and thought they obtained some results of value, but this method also has not survived.

In times of epidemics diphtheria antitoxin is, of course, extensively used for *prophylactic* purposes and rightly so, and while it is probably the only efficacious method in exist-

ence, to stamp out the disease *in situ*, especially when coupled with widespread quarantine, *the use of the antitoxin is absolutely without effect upon the persistence of the bacilli and the carrier state*. On this point the verdict is quite unanimous. Prip³ in particular mentions that the use of antitoxin, given for curative purposes, has not the slightest effect upon the continued existence of the bacilli in the fauces. That this should be so really stands to reason, if we remember that the serum in question is purely an antitoxic serum.

The reason why all these various methods of treatment do not lead to the desired end is unquestionably because the principal foci where the organism vegetates cannot be reached in such a manner. In the past we have thought of the bacilli as existing upon the mucous *surfaces* of the throat and nose, but evidence is rapidly accumulating that the organisms which are here present have reached these surfaces only more or less accidentally, and that the actual foci of development are located below the surface in various nooks and corners, where local applications could scarcely reach them. Here, no doubt, in the majority of cases they gradually fall prey to the normal and natural defenses of the body, or die in consequence of lack of suitable nourishment, or they may be crowded out by other bacteria. But, as we have seen, they do persist in some, and in the management of these cases the best course to pursue, aside from the education of the victim, is to attempt to find their hiding place and to eradicate this as thoroughly as possible. Whether or not this can be accomplished will, of course, depend upon the individual case, but there can be no doubt that the best chances of ridding the individual of his fatal possession lie in this direction. As yet comparatively little work has been done from this point of view, but the little that has been accomplished is distinctly encouraging. Albert³⁰ thus relates that in the course of an outbreak of the disease in the University Hospital of Iowa City, a number of carriers, who had been isolated, attempted to bring about their release by using a disinfectant gargle within fifteen minutes of the time that cultures were to be taken. In five of the eight individuals the cultures from the surface were then actually negative, whereas all but one

culture from the crypts of the tonsils were positive. The writer then reports that he succeeded in ridding all of the fourteen cases of their bacilli by treatment of the crypts of the tonsils with a 5 to 10 per cent. solution of nitrate of silver, which was applied by means of a thin, flexible applicator, and he adds that a number of physicians to whom he recommended this treatment had informed him that this method yielded better results than any other that had been tried. In his own series of cases the organisms disappeared within three days. Unfortunately the writer does not state whether any or all of the cases were temporary or chronic carriers, but even if they were temporary carriers only, the results achieved in so short a time are certainly very encouraging.

Kretschmer³¹ reports that he was able to free from the carrier condition thirteen patients in whom the more simple methods had failed, by squeezing the tonsils and forcing the plugs of detritus out of the crypts.

Surgical Treatment.—While these methods may be applicable in the case of temporary carriers, and mark an advance in our methods of treatment, in so far as they attempt to eradicate the niduses of bacillary development, rather than to treat the organisms that happen to be located on the surface of the epithelial lining of the fauces, they will scarcely suffice to rid *some* chronic carriers at any rate of their organisms. Dr. Hogan, who had charge of the Sydenham Hospital for contagious diseases of Baltimore, has thus related to me the case of a young woman in whom all applications, even injections of nitrate of silver into the substance of the tonsils, were in vain.

The individual was a chronic carrier who had been responsible for an outbreak of diphtheria in a local reformatory and had been kept in quarantine, under treatment most of the time for one hundred and thirty-six days. Finally it was decided to remove her tonsils and thirty days later she could be discharged, after repeated cultures had shown that her carrier condition had come to an end. A similarly satisfactory result was obtained in another case in whom the carrier state had followed an attack of the disease. It is noteworthy

in connection with the first case that the tonsillectomy was performed without a preceding administration of antitoxin and that the wound healed without complications. Similar results have been obtained by others.

McCord, Friedländer and Walker³⁴ report that at Camp Sherman tonsillectomy was carried out in a number of cases with a quick termination of the carrier condition in all. Even if tonsillectomy may not be necessary in all cases, it is suggested to refer every carrier to the throat specialist nevertheless for treatment of any ulcers or crypts in the tonsillar or adenoid tissue. The same observers speak favorably of the use of an 0.25 per cent. aqueous solution of chloramin-T (chlorazene) as a gargle (three or four times daily), followed by an oily spray of dichloramin-T, of 2 per cent. strength. They found that by systematizing the treatment of the carriers along these lines, it was possible to return them to duty after an average of only twenty-three days in the hospital, whereas before that time this was fifty-five days for diphtheria cases that had become convalescent carriers.

Keefer, Friedberg and Aronson³⁶ have reported similar successes from Camp Doniphan. They found that of 294 carriers in whom tonsillectomy was performed 94, or 32 per cent. only, gave negative cultures immediately after the operation; 136, *i. e.*, 46.4 per cent., became negative by the end of the first week; 38, or 12.9 per cent., by the end of the second week; 11, or 3.7 per cent., by the end of the third week; 14, or 4.7 per cent., by the end of from four to eight weeks, while a single case proved refractory altogether.

Such results show that the carrier problem so far as diphtheria is concerned is not only theoretically, but under military conditions at least practically, also capable of a satisfactory solution, in a large number of cases, but I fear that in civil life we are as yet very far from that goal.

In those cases in which the tonsils can be excluded as the habitat of the bacilli, the discovery of their hiding place may, of course, be attended with great difficulties, and their eradication be impossible. As a matter of fact, military surgeons have found that the nasal carriers are the most difficult to treat, and that in many of those showing atrophic rhinitis and

infected sinuses a cure can hardly be expected. A great ideal of further work thus still remains to be done, but I believe that as soon as the idea is once definitely abandoned, that in the carrier the organisms "grow on the surface," and it is realized that it is essential to search for their focus or foci of development, real headway in the cure of these people will be made. In the meantime, of course, we must handle the carrier problem as best we may. Most important naturally, as I have already pointed out, is the determination whether or not individuals who have recently passed through the disease, as well as those with whom they have been in contact, are carriers. This is purely a bacteriological problem and is to be solved by bacteriological methods (see above). When once the diagnosis has been made, quarantine and local treatment are next in order, coupled with adequate instruction of the individual regarding the danger which he represents through contact with other people. If the persistence of the organisms should unfortunately stamp the individual as a chronic carrier, the quarantine must, of course, be lifted, as it is manifestly out of the question to hold the person indefinitely. Much will henceforth depend upon his own good sense and good will, and if both be good he may prove of but slight danger to his entourage. But in any event it will be essential to keep such a person under supervision. He should be compelled to report from time to time to the proper authorities, and his whereabouts should at all times be known, so that in case of an outbreak of the disease it can be determined whether he could possibly have been the causative agent. So long as this does not occur he may remain at liberty. If, however, it can be shown that through his own carelessness he has brought about an outbreak of the malady, it would seem proper to confine him under surroundings where he cannot do any harm. Like carriers of other disease germs, he should under no circumstances be permitted to engage in the handling or preparation of foodstuffs, excepting in his own family and then only, if it is absolutely imperative.

As the susceptibility to diphtheria is particularly great in children it would also suggest itself that the carrier be excluded from contact with children as far as possible. This

would apply particularly to school teachers and to nurses and attendants in hospitals and similar institutions.

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PLAGUE.

WHILE there is no evidence to show that the *bubonic type of plague* is ever transmitted from man to man,¹ the contagiousness of *pneumonic plague* is well known, and the question naturally suggests itself whether carriers may not play a role in the dissemination of this type of the malady. Unfortunately we are not yet in a position to speak definitely on this point, but so far as the available evidence goes, it would seem that *pneumonic plague* may indeed be transmitted in this manner.

Active Carriers.—Gotschlich² has thus reported two cases of secondary and one case of primary plague pneumonia, in which virulent plague bacilli could be demonstrated in the sputum several weeks after convalescence. In the first case the pneumonia developed on the fifth day of the disease. The patient left his bed for the first time on the thirty-fourth day, and was continuously up and about after the sixtieth day. But notwithstanding, bacilli were demonstrable in the bit of sputum which the man could furnish, as late as the seventy-sixth day. In the second case plague bacilli were demonstrated in the sputum by animal experiment twenty days following a return to normal temperature, and six days after the patient had definitely left his bed. In the third case, which was a primary plague pneumonia, the patient was continuously up and about after the twenty-second day, and although his sputum scarcely differed from ordinary saliva in appearance, it nevertheless contained virulent bacilli as late as the forty-first day. These findings, of course, prove beyond a doubt that convalescents from plague pneumonia may be carriers for a time sufficiently long to infect others, providing, of course, that the retention by the organisms of their virulence for the experimental animal implies that human beings also would be subject to infection.

Since Gotschlich's initial observations similar findings have been reported by other investigators. Vagedes³ thus mentions a case in which the bacilli persisted in the lung for two months, though it must be mentioned that the patient was continuously febrile. Voges⁴ cites an instance in which the organisms were demonstrable in large numbers four weeks after the beginning of the disease, and when the patient had been convalescent for some time.

Métin,⁵ on the other hand, was unable to demonstrate plague bacilli in the sputum of plague pneumonia convalescents after the ninth afebrile day, and he relates that during convalescence their virulence seemed to be diminished. He nevertheless regards such cases as exceedingly important from an epidemiological standpoint.

Schottelius,⁶ further, has pointed out that in addition to the pneumonic form of the disease, there exists also a bronchitic type running a course of greater or lesser intensity, in connection with which he was able to demonstrate the presence of plague bacilli in the sputum in large numbers, and he rightly regards the lighter forms of this type as particularly dangerous, as their true nature would not be suspected without a bacteriological examination.

Passive Carriers.—While there can be no doubt that convalescents from plague pneumonia may harbor and eliminate the corresponding organisms in their sputum for a time sufficiently long as to warrant their classification as active carriers, there is thus far no evidence to show that the disease may also be transmitted through the intervention of passive carriers. Strong⁹ and his collaborators state that there is no definite bacteriological evidence that healthy carriers of the disease with plague bacilli in their sputa existed during the Manchurian epidemic of pneumonia plague of 1910-11, but he mentions that they had occasion to examine only two persons who were suspected of being carriers of this order.

There are a few observations which go to show that an individual may harbor the organisms in his sputum for several days preceding the outbreak of the malady in his own person,^{7 8} and it goes without saying that such individuals may be dangerous to others. But they cannot be viewed as

proper carriers in the sense in which we usually employ the term, unless it could be demonstrated that such persons harbored the organisms for a period that extended beyond that of the incubation of the malady.

Mode of Infection.—From the standpoint of prophylaxis it is, of course, clear that any person who eliminates plague bacilli in his sputum should be treated exactly as a plague pneumonic, and that no individual who has suffered from this type of the malady should be released from quarantine until repeated bacteriological examinations have shown that he is not a carrier. It has been argued inasmuch as plague pneumonia *ordinarily* occurs in only about 2.5 per cent. of all bubonic plague cases, that individuals suffering from this form of the disease are a negligible factor in the dissemination of the malady; that an epidemic of human plague always presupposes the existence of acute rat plague, and the transference of bacilli from infected rats to human beings through the agency of the rat flea. On the other hand, the belief has been expressed that a rat epidemic cannot be initiated through fleas that have been infected by biting human beings, the principal argument against such a possibility being the fact that the amount of blood which the insect could take up from the human being would not contain a sufficient number of bacilli to bring about the infection of a rat through natural methods.* However this may be, it must be admitted that plague may at times show a much more marked tendency to assume the pneumonic form than is ordinarily the case, so much so, in fact, that one can speak of actual epidemics of plague pneumonia (*e. g.*, the Manchurian epidemic of 1910–11), and by such patients the plague bacilli are disseminated in huge numbers.⁹ This being the case it would suggest itself that rats might very well receive a surface infection of their skin from such a source, sufficient in extent to lead to an outbreak of the disease, if such animals were then bitten by a flea. We must remember that the con-

* Strong and his collaborators found, on the other hand, in plague pneumonia that in many instances the bacteria are present in the blood in very large numbers, so that a diagnosis can often be made from a single microscopic examination.

clusion has been reached that the *ordinary* rat epizootic is initiated through the infection of an individual rat in consequence of a flea's biting through an area of skin that has previously been soiled by the discharges of an infected flea, and if this be so it would certainly suggest itself that the same result would follow if the surface contamination of the rat's skin had occurred through soiling with the sputum of a human plague pneumonic, either directly or indirectly, in the form of dust. Should future investigations show that this is possible it would also follow that a *convalescent* from plague pneumonia might initiate a rat epizootic and thus indirectly give rise to an epidemic of the ordinary type of plague.

Recognition of Plague Carriers.—*Animal Experiment.*—The recognition of plague carriers is effected most readily by inoculating rats subcutaneously at the root of the tail with a small quantity of the individual's sputum, or the discharge from broken down glands, suitably emulsified with a little saline. If plague bacilli be present death invariably results within ten days, the animals presenting characteristic lesions which are readily recognized with the naked eye, viz., engorgement of the subcutaneous vessels, pink coloration of the muscles, and the presence of bubos which are surrounded by an area of marked injection, with occasionally hemorrhagic infiltration. The gland itself is firm, but usually caseous, and at times hemorrhagic. The liver appears stippled and as though dusted with pepper. Pleural effusion, when present, is especially characteristic. The spleen is much enlarged, friable and often speckled like the liver.

Bacteriological Examination.—Cultures should be prepared from the bubo, the heart blood, the spleen and the liver, for which purpose ordinary meat infusion broth, layered with a little sterile oil or butter, and meat infusion agar—the latter containing 3 per cent. of sodium chloride, will be found best. The reaction should be neutral or slightly alkaline. The specimens should be incubated at a temperature of from 25° to 35° C.; above 38° growth is much delayed. During its growth in bouillon, which takes place slowly, the organism forms flakes or flocculi which rapidly sink to the bottom of the tube, leaving the supernatant fluid clear. Stalactite or

stalagmite formations may also be seen starting from the walls of the tube or from the suspended droplets of oil or butter. On agar after twenty-four to forty-eight hours, the colonies are small, delicate, transparent, dew-drop like. After forty-eight to seventy hours they have become larger, raised and less transparent. Mucin production is variable.

In stained preparations the characteristic appearance of the organism is that of a short, more or less ovoid bacillus, swollen in the center and rounded at the ends, whose polar regions are readily stained with dilute carbol fuchsin or borax methylene blue* (one-half minute), while the interpolar area remains colorless. They appear singly, in pairs and sometimes in short chains. To bring this out the smears should be fixed by absolute alcohol, and not by heat.

On agar, involution forms are obtained among which there are long, slender, segmented bacilli of vacuolated appearance, while others resemble yeast cells, and still others appear club shaped. Many of the involution forms stain only very imperfectly, and sometimes only a portion of the organism takes up the dye. The organism is negative to Gram. In hanging drop preparations no true motility is noted. Tested against antisera which have been prepared by immunizing rabbits with living, *avirulent* plague bacilli, administered intravenously, agglutination is observed in 1 to 80 dilutions (using 0.5 per cent. saline as diluent, and for the purpose of emulsifying the organisms), when the organism is isolated from infected guinea-pigs, while when cultured from human lesions, the same result is obtained in dilutions varying between 1 to 160 and 1 to 1280, according to the nature of the strain. The period of observation should be from two to four hours, and controls set up with normal rabbit serum.

Management of the Carrier.—*Quarantine.*—While the Indian Plague Commission of 1908 concluded "that there is no evidence that man harbors the bacilli after he has recovered from the disease," and while there is apparently no danger of man's conveying the malady to non-infected districts, excepting through the agency of transported infected rat fleas, it would seem advisable nevertheless to *quarantine*

* The solution is a 2 per cent. solution of methylene blue in 5 per cent. borax water.

plague cases until bacteriological examination has proved that any discharge from the seat of the malady, at a time when the patient is otherwise well enough to leave the hospital, is actually free from plague bacilli. It is, of course, well known that in the majority of cases no *living* bacilli can be demonstrated in the pus of the bubos, by the time that they break through the skin, but that this is not invariably the case has also been shown.¹⁰

So far as the *management of plague carriers of the respiratory type* is concerned, the same regulations should, of course, apply to these, as to actual plague pneumonia, and to diminish the chances of the production of carriers of this order, irrespective of the elimination of danger to the patient's entourage, the latter should be capped, gowned and masked, and as Strong and his collaborators have suggested, protected with goggles. Hospitalization of the patients themselves is, of course, absolutely essential and should be carried out whenever possible, and as the organisms seem to be able to persist outside of the body for a considerable length of time, in dust and on fomites of all kinds, the liberal use of disinfectants must be regarded as one of our most important methods of defense.*

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* Strong and his collaborators have pointed out that the sputum from pneumonic plague is no longer infectious when thoroughly dried, but that when frozen and pulverized, particles of it may be blown about and remain infective for long periods of time, or until the sputum is again thawed.

TYPHOID FEVER.

THE impetus to the splendid series of investigations which culminated in the recognition of the important role which carriers play in the dissemination of typhoid fever was given by Koch¹ in 1902. Basing his conclusions upon the findings collected by the Typhoid Commission of Trier, in the course of the preceding nine months, he expressed the belief that the propagation of typhoid fever took place essentially through the transference of the corresponding organisms from individual to individual, and that while infected drinking water *could* unquestionably produce the disease, infection of the water by a typhoid individual must inevitably precede and that a non-infected even though bad water in itself can have nothing to do with the production of the malady. He maintained that in the past too much emphasis had been placed upon the possibility that certain periodical outbreaks of the disease—notably in so-called typhoid houses and typhoid districts—might have been due to the activity of typhoid organisms which had been lying dormant possibly for years, in soil and ground water, and which then through water-courses had found their way into the drinking-water supply and thus brought about the outbreak. As a matter of fact, the origin of many outbreaks, notably those of a local character, seemed in those days so completely wrapped in obscurity, that the assumption of a possible latent existence of the organism, viz., an existence outside of the human body, did not appear unwarrantable, even though unsupported by tangible evidence. Certain bacteriologists, in fact, expressed the belief that the typhoid bacillus might develop directly from the colon bacillus through a process of mutation and that some of the obscure outbreaks of the malady might be accounted for upon this basis. Suffice it to say that the possibility of such a transformation has not been demonstrated and need

not be considered from a practical standpoint until such a demonstration has actually been made.

Koch's dictum, as outlined above, was, however, not only based upon the results of epidemiological studies *per se*, but further supported by observations on the part of various investigators, to the effect that typhoid bacilli may be found in the gall-bladder and abscesses of various organs, many years following an attack of typhoid fever, and that they may be present in the feces and urine of typhoid convalescents. Isolated observations of this order had been made already by Neufeld² and others, but in these cases the organisms ultimately disappeared, as the patients regained their full strength.

Active Carriers.—In the course of the investigations, which were made at Trier, referred to above, Frosch³ encountered certain individuals who had passed through an attack of typhoid fever, in whom the organisms persisted—in other words, individuals in whom a bacteriological recovery did not coincide with or even follow clinical recovery. It is to be noted that Frosch fully realized the significance of these findings, and emphasized their importance at the meeting of the directors of the various Typhoid Stations which the Prussian Government had established at Koch's solicitations. At that time he supported his belief that such individuals might play an important role in the dissemination of the disease by similar findings which had been noted by v. Drigalski⁴ and Dönitz.⁵ The former had an individual under observation at the time, who ever since his clinical recovery from typhoid fever, four months before, was still eliminating typhoid bacilli in the feces.*

Dönitz's patient was a woman in whom typhoid bacilluria still existed nine months after recovery.

An enormous amount of work then followed which was largely carried out at the Research Stations established at Trier, Saarbrücken, Idar, Metz, Strassburg and Landau. This work is prominently connected with the names of Lentz,⁶ Drigalski,⁷ Frosch,⁸ Forster⁹ and his collaborators,

* This person was evidently a permanent carrier, as the elimination was still noted one and three quarter years following recovery from the disease.

Levy,¹⁰ Blumenthal,¹¹ Fornet,¹² Kayser,¹³ Klinger,¹⁴ Minelli¹⁵ and many others.

The immediate results of these investigations thoroughly supported the opinion expressed by Koch, that in the dissemination of typhoid fever the typhoid convalescent plays a most important part, and fully established the status of the typhoid carrier as we understand it today.

Duration of the Carrier Stage.—It was shown by Drigalski⁷ that typhoid bacilli are eliminated in the feces either continuously or periodically by a large number of the patients during the active period of the disease, the percentage ranging from 15.6 during the first five days to 11.5 during the fourth week, and that in fully 11 per cent. of the individuals this continues into the period of convalescence, viz., the eighth to the tenth week; in other words, that in point of time clinical recovery precedes bacteriological recovery. In the majority of normal cases the latter takes place after eight to ten weeks, dating from the beginning of the disease, and in those complicated by relapses eight to ten weeks following the last relapse. During the stage of convalescence the individual may accordingly be viewed as a carrier. This type, however, is not to be confounded with those rarer cases in which the elimination of bacilli continues beyond the tenth week. While it is admitted that bacteriological recovery may take place even then, this is exceptional, and in the majority of cases the elimination of the organisms in question continues practically indefinitely. In the series of 400 typhoid cases analyzed by Lentz there were only six in whom the ten-week period was exceeded and bacteriological recovery still occurred, the time ranging between three and a half and nine months. Fifteen out of the total number, *i. e.*, 3.75 per cent., apparently became *permanent carriers*. The assumption that the condition was actually a permanent one was based not only upon the findings obtained in connection with the cases which had developed during the duration of the existence of the Commission, but also upon the results obtained in connection with the examination of individuals whose typhoid attack antedated that period.

The other observers taking part in the investigation obtained similar results.

Passive Carriers.—At the Strassburg Station during the period from July 1, 1903, to March 31, 1905, 23 carriers were discovered, which Klinger¹⁴ reported in 1906; 11 of these gave no history whatsoever of a preceding attack of typhoid fever. They were encountered in the course of an examination of 1700 supposedly healthy individuals, who, however, had been in contact with typhoid patients. This would correspond to a percentage of 0.64. In all of these the appearance of the typhoid bacilli in the discharges was temporary. In 9 of the 11 the organisms were found only once; in the tenth case three times in the course of a fortnight, and in the eleventh twice in the course of a month. The remainder, viz., 12, were true permanent carriers; 8 of these had developed the carrier condition while under observation in connection with an attack of typhoid fever. As the total number of typhoids under investigation during that time was 482, the percentage of resultant chronic carriers would be 1.7 as contrasted with 63, *i. e.*, 13.1 per cent., of temporary carriers.

All of the carriers observed by Klinger were *fecal carriers*, though it is to be noted that in eight the organisms were also found in the urine—*urinary carriers*. The writer mentions particularly that the number of bacilli in the latter was always small and that a bacteriuria such as one frequently sees *in the course of the malady and during convalescence*, with millions of organisms to the cubic centimeter, was never observed. Carriers of this order have been described by practically all investigators of the problem. One of the earliest observations of the kind was made in 1900 in our own country, by Brown,¹⁸ who reported the case of a woman in whom a cystitis developed on the ninth day following an abdominal operation, and in whom it was thought that the typhoid bacillus was accidentally introduced by catheter. It is to be noted, however, that the woman had had typhoid fever thirty-five years previously, and in view of our present knowledge it is more likely that she was a carrier during all this time than that she was infected with a catheter—at one of the most up-to-date institutions of our country. Young¹⁹ described another case of this type in 1901. In this patient

a cystitis developed during an attack of typhoid fever "owing to infection with the typhoid bacillus," and the organism could still be demonstrated in the urine after seven years. In the same paper Young reported two additional cases of chronic cystitis due to the typhoid bacillus.

Commenting on his own cases of typhoid bacilluria Klinger remarks that 7 of the 8 were women, and that it is easily conceivable that the organisms found their way from the anus—all of them passed typhoid bacilli in the feces—to the vulva, and were then mechanically washed away by the urine, in specimens of which they could multiply, thus readily leading to their discovery. That such a possibility exists may be conceded, and in two of his cases it is supported by the finding of a sterile urine when this was obtained by catheter. On the other hand, such an explanation would only be warrantable if a catheterized specimen could be shown to be sterile.

Intermittent Elimination of the Organisms.—The elimination of the bacilli in the feces is somewhat variable. During the course of the malady and the beginning of convalescence the organisms usually appear periodically—in *Schüben*, as the Germans say. Subsequently, when the chronic carrier stage has been reached the elimination tends to become continuous. Lentz has studied this phase of the problem with special care. He states that following a sharp ascent in the curve of elimination at the beginning of convalescence, this is usually followed by a corresponding drop or even an entire cessation in their elimination, but that beginning with the fourth afebrile week there is again a gradual rise which soon reaches a certain level which is thereafter maintained, subject to but inconsiderable fluctuations. Such at any rate appears to be the rule from which there are, however, not infrequent exceptions, and many writers warn insistently against the idea that a single or even several negative findings may be regarded as ruling out the carrier state. It is well to bear this in mind and to take such steps when investigating a doubtful case as will favor their elimination at the time. (See Recognition of Carriers.)

The number of organisms which is eliminated at one time is variable. On the one hand, not a single colony may be found on the plates; at other times there may be but one or two, while on still other occasions almost a pure culture is obtained, and this not only in different people, but in one and the same person. *As a rule* they are present in enormous numbers and demonstrable without recourse to the use of any "enriching" medium.

Tendency of Women to Become Carriers.—A very important observation which has been made by all observers is the marked tendency which women, and more particularly married women, manifest to become carriers. As a matter of fact, fully 82 per cent. of all chronic carriers are females, and even among the temporary carriers 60 per cent. are of that sex. Children, on the other hand, while they represent 35 per cent. of the temporary carriers, only become chronic carriers to the extent of 4 per cent. The remarkable tendency of women to become chronic carriers is particularly important, if we bear in mind their intimate association with the handling and preparation of food (see below).

Habitat of the Organisms.—Regarding the probable focus at which the bacilli that appear in the feces develop, a great deal of excellent work has been done. v. Drigalski⁷ thus ascertained that the typhoid infection is by no means confined to the intestinal tract and its associated glandular organs. By cultural methods he showed that as one ascends the intestinal tract from the rectum the number of typhoid bacilli increases, and that in the duodenum and the upper portion of the jejunum one frequently meets with enormous numbers of typhoid bacilli in nearly or actually pure culture. In this respect v. Drigalski's findings agree exactly with those of Jürgens.²⁰ But he further made the interesting observation that a similar state of affairs exists in the stomach, where the organisms could always be demonstrated in large numbers, in spite of the prevailing acid reaction, whereas frequently it was most difficult to demonstrate the organisms at all in the bases of the intestinal ulcers—contrary to what one would have expected according to our former notions. v. Drigalski further demonstrated their presence in the

esophagus, in the coating of the tongue, in the tonsils, in the lungs, in the trachea; in short, in practically all organs of the body, but in addition also—and this interests us particularly—in the bile, where they could always be found.

Corresponding observations on the occurrence of typhoid bacilli in the bile passages had previously already been made by a number of observers. Anton and Fütterer²¹ had thus demonstrated the presence of the organisms not only in the gall-bladder but also in gall-stones. Chiari,²² and Chiari and Kraus²³ reported their frequent presence in the bile following typhoid infection, and Kanthack,²⁴ like v. Drigalski, had encountered them in every instance. These older observations now gained new importance.

Regarding the manner in which the organisms reached the gall-bladder there was uncertainty. The prevailing view had been that they gained access from the intestines through the common duct. Blachstein and Welch,²⁵ however, showed in the animal experiment that the organisms appear in the gall-bladder following intravenous injection, and that they may be demonstrable here after a long while—in one instance after 128 days—and at a time when all other organs are sterile. These results were fully confirmed by Doerr,²⁶ who also could demonstrate the organisms after 120 days, but he points out that such a long-continued existence in the gall-bladder was exceptional, and that after a certain length of time they usually disappear. He suggests that the duration of their sojourn in the gall-bladder may be dependent upon the extent to which the walls of the latter become diseased. It is interesting to note that in no case was there an absence of inflammatory reaction, though at times this was slight. He adds that the blood and other organs were found sterile already after two weeks.

Such observations evidently fully justified the statement made by Chiari²⁷ at a meeting of the Section of Internal Medicine of the Association of German Naturalists in 1907, to the effect that typhoid bacilli enter the bile passages from the blood in every case of typhoid fever, that they produce inflammation and can then multiply indefinitely.

On the basis of these observations, which were further

supported by the long experience gained in the Pathological-anatomical and Bacteriological Institutes of Strassburg, Forster⁹ then expressed the opinion that *the gall-bladder constitutes the source of the fecal typhoid bacilli found in carriers.*

As regards the *modus operandi* by which the bacilli secure permanent lodgment in the gall-bladder, Forster expressed the opinion that their primary appearance in the biliary passages leads to a certain degree of inflammation, with consequent exudation. He seems to regard the latter as essential to the development of the organisms, and states that in pure bile they do not multiply, while bile mixed with a little serum constitutes an excellent culture medium. This, however, is in contradiction to the experience of other observers, such as v. Drigalski and Doerr, who noted that the typhoid bacilli grew readily though slowly and steadily in human bile. Doerr mentions specifically that so far as normal human bile is concerned there is no evidence whatever of a bactericidal effect, and it may be added that the same was noted when typhoid bacilli were inoculated into broth containing a mixture of bile and immune serum. Be this as it may, the fact remains that having once reached the gall-bladder they may here find lodgment and multiply indefinitely. In some manner, however, the process of inflammation is evidently of great influence upon the duration of their sojourn. Doerr, in connection with his animal experiments, thus noted that when the inflammation subsided, the bacilli also disappeared, while they remained if the inflammation continued. Irrespective then of the question whether exuded serum is essential to their growth, the fact remains that the inflammatory process in some manner has to do not only with their presence, but also with their continued presence. The correctness of this view can, of course, also be tested at the operating or the postmortem table in the case of chronic carriers who have passed through their typhoid attack long before. Levy and Kayser²⁸ seem to have been the first ones to report findings in this direction in a carrier whose condition had been recognized during life. This patient had typhoid fever in 1903 and developed the carrier condition at that time. Death occurred in 1906, and at the autopsy typhoid bacilli

were isolated from the contents of the inflamed gall-bladder in large numbers and in pure culture. Corresponding observations have since been made by many observers, such as Nieter and Liefmann,³⁰ Gould and Qualls,³¹ Bindsell,³² Hammond²⁹ and others. It is noteworthy that some of these writers dwell upon the thickened condition of the walls of the gall-bladder, and the fact that typhoid bacilli could be isolated therefrom. Their occurrence in this locality is interesting from two points of view: It suggests, on the one hand, that the infection of the contents of the gall-bladder may occur not only through the bile which enters through the cystic duct, but through the blood supply of the gall-bladder wall itself. On the other hand, it explains why drainage of the gall-bladder (*v. i.*) may be insufficient to remove the carrier state, and why cholecystectomy, other things being equal, is preferable to cholecystotomy as a method of treatment.

Association of the Carrier State with the Existence of Gall-stones.—As I have already pointed out, all investigators who have studied the problem of chronic carriers have noted the remarkable tendency of females in this direction. Forster⁹ thus found that of 194 *temporary* carriers, 29 per cent. were men, 45 per cent. women and 26 per cent. children younger than fifteen years of age, while of 173 cases of the *chronic* type, 79 per cent. were adult females and only 17 per cent. men and 4 per cent. children. It was this fact which caused Forster to suspect that a causal relationship might exist between the carrier condition and the development of gall-stones. The latter, as Rosenheim³³ first pointed out, and as has since been abundantly confirmed, is likewise much more common among women than in men (occurring in but one male to three females), while children are practically exempt. Just as the majority of gall-stone victims—about 90 per cent.—moreover, present hardly any or no symptoms, pointing to the existence of gall-stones, so also do fully 85 per cent. of the permanent carriers give no indication of disease of the gall-bladder, which nevertheless exists. This has raised the question whether the infection of the gall-bladder gives rise to the formation of the stones

or whether the existence of stones perhaps predisposes to the development or the continued existence of the carrier state. It is, of course, quite conceivable that an individual having gall-stones may at some time in the future be stricken with typhoid and ultimately become a chronic carrier, in which case the original cause for the development of the gall-stones would still remain in the dark. The first possibility therefore suggests itself as a more fruitful problem for investigation. A review of the literature from this point of view reveals a number of observations of great interest, which suggest that a typhoid infection of the gall-bladder may actually lead to the formation of stones. Doerr (*l. c.*) thus mentions that whereas gall-stones are never found in normal rabbits, he met with two concretions of the size of a lentil, in one animal which had been injected intravenously with typhoid bacilli forty days before. He adds that typhoid bacilli were found in abundance in the interior of the concretions. He also cites certain findings by Richardson,³⁴ who succeeded in experimentally producing concretions in rabbits by the injection into the gall-bladder of agglutinated typhoid bacilli. The discovery of typhoid bacilli in the interior of human gall-stones, as first noted by Fütterer (*l. c.*), Blumenthal,¹¹ Levy and Kayser,²⁸ and since then by practically everyone who has taken the pains to make the requisite bacteriological examinations, coupled with the large number of clinical observations, to the effect that many individuals in whom gall-stones were found gave a history of typhoid fever in the past, and preceding the first appearance of symptoms referable to the gall-bladder, all suggest that an attack of typhoid fever predisposes to the development of gall-stones, particularly in females, and is probably responsible for their formation.

I have emphasized the association of typhoid fever with the development of gall-stones and the carrier condition for the reason that in a search for carriers special attention should be paid to individuals who complain or have complained of symptoms, however slight, in connection with the gall-bladder.

The important question, of course, arises whether typhoid bacilli which have once gained access to the intestinal canal can continue their existence here, irrespective of the con-

tinuation of the inflammatory process in the gall-bladder. Forster denies this possibility, while other observers, such as Lentz, suggest that they may do so, basing their opinion upon the enormous number of organisms which are usually found in the feces and the fact that they may appear in almost pure culture, which would suggest that they had crowded out the colon bacillus by their growth and had taken its place. The view that they cannot maintain themselves in the intestinal tract in the absence of continuous reinforcements from the gall-bladder is, however, more likely correct. That the organisms may multiply in the intestinal tract *for a while* and may even force the colon bacilli into the background is possible and indeed probable. But, if we remember the practical impossibility of artificially replacing the colon bacillus by other organisms, unless these are constantly supplied *anew*, as in the case of the *Bacillus bulgaricus*, it does not seem likely that the large numbers of typhoid bacilli in chronic carriers could develop without constant reinforcements. This is further suggested by the fact that the majority of typhoid cases do not become chronic carriers, notwithstanding the almost invariable presence of the organisms in the feces at some stage of the disease, and is also supported by the observation of cases in which following operation for gall-stones and evacuation of the gall-bladder the organisms disappeared both from the bile and the intestinal contents.

Dehler³⁵ mentions two cases in which he did a cholecystotomy, with the result that the carrying condition disappeared. Further investigations in this direction are, however, necessary, and it would seem well worth while to repeat the experiments of Blachstein and Welch and Doerr described above, and to supplement their studies by a control of the animal feces. In the postmortem room, moreover, the contents of the gall-bladder of every chronic fecal carrier should be carefully examined, with the idea in mind of determining whether a sterile gall-bladder could ever be associated with the presence of typhoid bacilli in the feces.

Virulence of the Organisms.—Another question that has suggested itself in connection with the carrier problem is,

whether or not the typhoid bacilli which we encounter in people who for the most part at any rate appear healthy and well, are actually virulent organisms and capable of infecting others. Bearing in mind the loss of virulence which certain organisms undergo when kept under artificial cultivation, a loss of virulence in the human being also, after thorough adaptation to its new surroundings, would, *a priori*, not seem impossible. So far as such a question can be answered by the animal experiment, the evidence is quite conclusive that there is no loss of pathogenic activity, as it has been shown that the limits of virulence in the case of carrier cultures are the same as with those obtained from the feces, the blood and the spleen of typhoid patients. Positive evidence of this order is particularly valuable, while negative evidence would in itself not have disproved the possibility that the organisms might after all have retained the same degree of virulence for the human being. Conclusive evidence of the virulence of the organisms in question for man is, however, afforded by the observation that many outbreaks of the malady have been traced directly to carriers.

It has been suggested by Hilgermann³⁶ that the relative infrequency of infections in the entourage of carriers may be due to variations in the virulence of the organism and that this diminishes with the continued parasitic existence of the latter in the organs of its host. As a matter of fact, there is no experimental evidence to support such a view, and it is negative, moreover, by the observation that the carrier can infect throughout a long period of years. Hilgermann's further suggestion that infection can only occur through a carrier if a special predisposition exists on the part of the recipient, while likewise unsupported by experimental data, seems more reasonable. But, on the other hand, one must not forget that the carrier's fingers need not always be contaminated, and, moreover, that even though contaminated, they might not always carry an infecting dose, and that even though the quantity be sufficient for the infection of one individual, its distribution in the food and among several recipients would tend to diminish it sufficiently to prevent infection.

Numerical Relation between Carriers and Cases of Typhoid Fever.—Before passing on to a recital of outbreaks, which have been traced to the activity of carriers, we shall briefly consider what knowledge we actually possess regarding the numerical extent to which carriers have been proved to be responsible for the dissemination of the disease. It may be stated in advance that our knowledge in this respect is as yet quite meager, owing to the insignificant part which health department laboratories in many countries have thus far taken in the study of sanitary problems. The figures obtained at the various Stations established by the Prussian Typhoid Commission show conclusively, however, conservative as they are, that the carriers play a very important role in the dissemination of the disease. It will be recalled that only a relatively small number of typhoids become chronic carriers, but that even so they are sufficiently numerous as to constitute from 0.3 to 0.4 per cent. of the total population of any large city. Calculated out for a city such as New York, this would correspond to approximately 25,000 cases! With such an enormous number of carriers at large, one is on first thought surprised that typhoid is not much more prevalent than is actually the case. But we must remember that the location of the bacilli in the intestinal tract or the urine renders their dissemination among human beings much more difficult as compared with other organisms which are distributed through the discharges from the throat and nose, so long as distribution by a common commodity such as the water or milk supply can be eliminated. The chances of infection through *direct contact* with the patient and his immediate surroundings are, of course, much greater than through the carrier. At the same time there is greater *indirect* danger from a carrier for the reason that the number of persons with whom he is brought into contact is certain to be larger than would be the case in a sick room. In a study of a large number of cases we accordingly find that the majority of typhoids have acquired the disease through contact with typhoid patients, but that of the remainder a very considerable portion can be referred to carriers.

Regarding the actual percentage of such cases as compared

with the total number, there is, however, a great deal of uncertainty. Frosch³⁷ in an analysis of 978 cases which had been fairly definitely traced to their source of infection found that 642, viz., 65.04 per cent., were contact cases. In 104 the question was still an open one whether the infection had occurred through direct or indirect contact, but as 3 cases had developed among persons who had been living in more or less intimate association with typhoid patients the writer thinks these should be added to the number of contacts, which would increase the percentage to 76.2. There remain then 232 cases, viz., 23.7 per cent., which were attributable to indirect infection—through drinking water, bathing, milk and other articles of food. Of the 746 cases, only 49 could be referred to carriers, *i. e.*, only 5.01 per cent. of the definitely traced cases. This low percentage, on first consideration, would suggest that the danger from the carrier was relatively slight, but it must not be forgotten that Frosch's series of 978 traced cases corresponds to a total of 2080, and hence represents but 47.7 per cent. of that number, leaving 52.3 per cent. unexplained. The data from which Frosch's figures were drawn were obtained by sending out a questionnaire and analyzing the returned answers. It does not require much imagination to recognize why the majority of the "traced" cases should have been contact cases pure and simple and not due to carriers, for it is evident that a second case occurring in the surroundings of a first case would naturally be attributed to this source, while the answer as regards the origin of the latter would most likely have been "unknown." But it is just the "unknowns" which we must look upon with special suspicion as being possibly due to carriers, and if we bear in mind the difficulty which is so often experienced in finding the carrier, and the fact that when he is found he is so often proved responsible for a larger number of infections than the patient who is confined to bed and in contact with only a small number of people, we will also realize that definite conclusions regarding the actual role of the carrier in the distribution of the disease can certainly not be reached by an analysis of information that has been collected in such a manner. As a matter of

fact, Frosch's data do not accord at all with the findings obtained at Strassburg, as the result of an actual investigation of concrete cases.

At the Strassburg Station 386 cases of typhoid fever were studied from January, 1906, to the end of June, 1907. Of these, 77 cases, *i. e.*, 20 per cent., could be traced to carriers; 117 cases, *viz.*, 30 per cent., were regarded as contact cases, while in 45, *i. e.*, 11 per cent., the source of the infection could not be determined. The remainder were caused by infection through drinking water, milk, etc. By distributing the unexplained 11 per cent. among the three groups the carrier class would be increased to 22 per cent. This figure, however, does not yet express the full extent to which carriers are responsible for the dissemination of the disease, for of the water and milk cases a large number are now definitely known to be due to carriers. If we distribute these between the carriers and contacts in the proportion of two to three, the carrier percentage would be increased to 40, which would seem a conservative estimate, and would indicate what a formidable factor they represent in the dissemination of the disease. These figures applied to the typhoid cases occurring in a city like New York would indicate that for 1914, for example, 1004 were referable to this source. As I have said before, the healthy carrier is far more dangerous than the patient. In the case of the latter the danger is a manifest one, while in the case of the former it is hidden.

Manner of Infection.—Regarding the manner in which the carrier can infect others, many possibilities, of course, exist. Whenever infected fecal material or urine finds its way into the drinking water of a community, ideal conditions naturally exist for the development of epidemics, the extent of which will be proportionate to the number of people using the water. In districts in which sewage is used for the purpose of fertilizing farms or gardens, outbreaks may be expected among those using uncooked products in their diet. In the past it was customary among agriculturalists to sprinkle their lettuce with sewage in order to keep it "fresh," and many outbreaks of the disease have been traced to such a source. The peculiar danger of the carrier, however, which

distinguishes his type of infectiousness from that of the typhoid patient, lies in his relation, through *direct contact*, with the food supply of a community. We thus find that on farms it is the carrier milking the cows who is so frequently responsible for outbreaks of the disease, the extent of which may equal that referable to infection of the water supply. In institutional outbreaks or in house epidemics similarly we frequently find the cook to be the responsible factor, which means, of course, that the individual has soiled his or her hands with fecal matter or urine and has transferred the responsible organisms to the food. The amount of harm which a single individual can thus cause is perfectly amazing. In a recent analysis made by the Division of Preventable Diseases of the Minnesota State Board of Health,³⁸ in the case of 37 carriers, it was found that 220 cases of typhoid fever, including 12 fatalities, could be traced to such individuals, giving an average of 6 cases per carrier. In the case of the now world-famed Typhoid Mary³⁹ of New York, 57 cases of the disease with 3 deaths could be traced to this one carrier. In one instance related by Kossel,⁴⁰ an outbreak of 25 cases was found to be due to a single carrier who was employed on a farm which furnished milk to the stricken individuals.

Examples Illustrating the Activity of Carriers.—To pass on to a recital of a number of concrete cases illustrating the connection between outbreaks of the disease and carriers, I would head the list with the record of Typhoid Mary, to which I have just referred.

*The Case of Typhoid Mary.*³⁹—The earlier portion of this woman's history has been related by Park in the third edition of his *Pathogenic Microorganisms*, published in 1908, and reads as follows:

"Five years ago a visitor of the family in which the woman was cook developed typhoid fever some ten days after entering the household. The cook had been with the family for three years, and it is difficult to judge which infected the other. In 1901 the cook went to another family. One month later the laundress was taken ill.

In 1902 the cook obtained a new place. Two weeks after

arrival the laundress was taken ill with typhoid fever; in a week a second case developed and soon seven members of the household were sick.

In 1904 the cook went to Long Island. There were four in the family, as well as seven servants. Arrived June 1. Within three weeks after arrival four servants were attacked. The servants lived together.

In 1906 the cook went to Oyster Bay. Between August 27 and September 3 six out of eleven in the house were attacked with typhoid. At this time the cook was first suspected. She went then to Tuxedo and remained there from September 21 to October 27. On October 5 the laundress developed typhoid fever.

In 1907 at New York, two months after the cook's arrival, two cases developed, one of which proved fatal. Altogether during five years this cook is known to have been the cause of twenty-six cases of typhoid fever.

She was removed to a hospital March 19, 1907. Cultures taken every few days showed bacilli off and on for fourteen months. Sometimes the stools contained enormous numbers of typhoid bacilli and again for days none would be found.

The woman then appears to have escaped from observation until 1914. In October of that year she was engaged as cook in the Sloan Hospital for Women of New York. In January and February of 1915 an outbreak of typhoid fever occurred, principally among the nurses, doctors and help of the institution, involving twenty-five cases.

A careful investigation into the food and water supply of the hospital showed no evidence of outside contamination.

Fecal and Widal specimens were then taken from the entire kitchen and pantry force, but nothing was found beyond a faintly positive agglutination reaction in the case of the cook, who gave a history of having had typhoid fever a number of years before. Three fecal specimens from her were examined at the hospital, but no typhoid bacilli found. The woman then left the premises on a few hours' leave and did not return or leave her address. She was located, however, with a great deal of difficulty and specimens of her feces obtained, which she submitted under an assumed name and while she believed

that she was eluding the Health Department. While under observation she aroused the suspicions of the Health Department, and it was surmised that she might be the famous Typhoid Mary (Mary Mallon). Investigation established that this was indeed the case. She was then taken to Riverside Hospital and carefully investigated, the findings proving conclusively that she was a chronic typhoid carrier.

A subsequent study of her career showed that she had infected still other individuals beyond those already mentioned, and that she may have given rise to the well-known water-borne outbreak of typhoid fever in Ithaca, N. Y., in 1903, embracing over 1300 cases. As a matter of fact it could be shown that a person by the name of Mary Mallon had been employed as a cook in the vicinity of the places where the first case appeared and from which the contamination of the water supply occurred.

Another interesting instance illustrating the danger of typhoid carriers to others has been reported by Ravenel⁴⁶ as follows:

In the fall of 1910 Mr. A. moved from Minnesota to the town of G., Wisconsin, bringing with him his wife and three boys. He bought a farm four miles northeast of the village. In December, 1909, Mr. A. had been operated on in St. Paul for pyonephrosis, and a tumor mass weighing five pounds removed. No bacteriologic examination was made. One of the doctors who assisted at the operation states that six months before he had treated Mr. A. for typhoid fever. About the time of moving to Wisconsin the eldest son had typhoid fever, and soon after the two other sons and their mother came down with the disease.

Mr. B., with his family consisting of his wife, two boys and a girl, moved from Minnesota to Wisconsin about the same time, having purchased a farm in the immediate neighborhood of Mr. A. While the buildings on this place were being put in order Mr. B.'s family stayed at the home of Mr. A., with the apparent result that first the daughter, and soon after Mr. B. and the two sons came down with typhoid fever.

In the fall of 1911 Miss C., a niece of Mr. A., came from St. Paul to teach in the public schools. She was in the habit

of spending the week-end at the house of Mr. A. After six weeks' residence in the town of G. she became ill with typhoid fever.

At the same time a sister of Mr. A. visited him and soon after returning to her home suffered from typhoid fever also.

About August 15, 1911, Mr. D. visited at the home of Mr. A. and took supper with him. September 20 Mr. D. entered a hospital after having been sick for some days and a diagnosis of typhoid fever was made. His illness began during the first week of September.

In the spring of 1912 two young men, E. and F., who were working at the home of Mr. A., both contracted typhoid fever.

In the fall of the same year Mrs. G., a sister of Mrs. A., accompanied by her son, spent a few weeks at the home of Mr. A. Soon after returning home both contracted typhoid fever.

In the latter part of 1912 or January, 1913, Mr. H., a brother of E., spent a night at the home of Mr. A., and twelve days afterward came down with typhoid fever.

In June, 1913, Miss I., a niece of Mr. A., living near him, suffered from typhoid fever. There had been frequent visiting between the two families.

On or about October 15, 1913, Mr. J. took the Rev. K., his wife and two children to the home of Mr. A. for a visit. They did not take a meal at the house, but the children became hungry and cookies were provided. October 28 the Rev. K. bought butter from Mr. A. for table use, and on November 2 Mr. A. and family dined at the home of the Rev. K. On November 11 the two children of the Rev. K. became ill with typhoid fever, and on November 30 Mrs. K. and her husband also went down with the disease, Mrs. K. dying.

It thus appears that 21 cases of typhoid fever occurred among persons in this community, or those who had visited there, and all of them had been in contact for longer or shorter periods of time with Mr. A.

In June, 1913, an investigation was made by the health authorities, and it was ascertained that Mr. A. and one son

gave a positive Widal reaction and that the urine of Mr. A. contained typhoid bacilli; cultures from the feces were negative. Subsequent examinations gave the same result. The water supply of the community was examined and found to be above suspicion, and there was no typhoid in the town except among those persons who had been in contact with Mr. A. As regards the manner of infection it would seem that this took place in the case of the Rev. K. and his family, at least, through some dairy products such as butter which the individual in question was known to have purchased from Mr. A.

Another interesting case which illustrates the important bearing which carriers have on milk epidemics is related by Kossel.⁴⁰

In the town of O. there occurred 25 cases of typhoid fever during the summer of 1906—3 about the middle of May, 5 toward the end of June, 6 about the middle of July and 11 about the middle of August; 21 of the 25 obtained their milk from the same dairy. The dealer in turn was supplied by three farms, one of which, B., had been under suspicion for a number of years. This farm furnished milk also to the town of F., where it had also been noticed that only those developed the disease who had been supplied from farm B. The health department had repeatedly investigated the situation, had made certain suggestions, which were carried out, but without producing the desired result—all this it may be added at a time when but little was as yet known of carriers. When attention was again directed to farm B. in connection with the outbreak of the disease at O., Kossel was asked to make an investigation along the new lines which had been suggested through the findings of the Prussian Typhoid Commission.

Farm B. was found to belong to village B., where epidemics of considerable dimensions had occurred in 1857 and 1872, since when the disease had never entirely disappeared, but had practically only attacked children and newcomers. The small river flowing through B. which furnished the drinking water supply had been suspected and wells sunk instead. The results were apparently beneficial, since laborers coming from outside, who in the past had usually developed the disease in from four to six weeks after their arrival, now rarely

became ill. That the disease had not been entirely eradicated, however, was shown by the development of 1 case in the month of January, 1906, and the outbreak in both O. and F. Some of the milk sent out from farm B. was mixed with milk from the village B., but as no village cases had occurred, save certain ones which might have been referred to the farm, the conclusion was reached that the farm itself constituted the source of the infection. The occurrence of the cases in O., in groups, suggested a *periodic* infection of the milk and not of the entire amount.

Specimens of fecal material were ordered from the fifteen employees on the farm. Examination showed that one of these contained typhoid bacilli in large numbers (October, 1906). The specimen in question came from a man whose duty it was to look after the pigs, but it was ascertained that he *at times* helped in milking the cows. The man had been employed on the farm for about twenty years. He gave no definite history of antecedent typhoid, but coming from the village B. it is quite conceivable that he had been infected there. The man was now removed from all contact with the dairy department and no more cases of typhoid developed thereafter until May, 1907, when 1 case appeared in the village B., and it was found that the same carrier had again been employed in the dairy. That the individual in question was a true chronic carrier was shown by the demonstration of typhoid bacilli in his feces on July 22, 1907.

An account of an extensive milk epidemic due to a single carrier has also been related by Bolduan and Noble.⁴¹ In this instance a sudden increase in the number of typhoid cases occurred toward the end of August, 1909, in the boroughs of Manhattan and the Bronx, and investigation showed that a certain milk supply was common to almost all. This was immediately shut off, but even so some 380 cases of the disease developed. Following the lead of the milk supply it was found that the infected milk came from Camden, N. Y., and that there had been an unusual prevalence of typhoid fever at this place for years. A tabulation of all the cases in the village in 1908 and 1909—27 in number—showed that 20 received milk from dairy X. The medical history of the dairy-

man's family revealed the following: The man himself had had typhoid fever in 1863 or 1864 (forty-six years ago). He came to Camden in 1866 and began to sell milk from the same dairy, as at present, in 1873. In 1878 his two-year-old daughter had "enteric fever." In 1886 his son-in-law, who was then working on the farm as a hired man, was very ill with a fever lasting several weeks—then termed "gastric fever." In 1893 another daughter was ill with "typhoid fever." In 1897 still another daughter was ill, in the fall of the year, with "intermittent fever," with which she was confined to bed for two or three weeks continuously, and which attack was followed during convalescence by a second attack, during which time the patient was very ill. In 1903 a hired man left the farm and was taken ill ten days later with "typhoid fever." In 1909 another hired man, while on the farm, sickened with typhoid fever and died.

An examination of the feces of the entire household was now made and revealed almost a pure culture of the typhoid bacillus in the case of the dairyman himself. Similar results were obtained a month later, and again after a year, so that the status of the dairyman as a chronic carrier, probably of forty-six years' duration, seems pretty definitely established.

The question now arose whether this particular man could be connected with the outbreak of the disease in Manhattan and the Bronx, which in turn had led to the investigation.

It was found that the man's son-in-law was also engaged in the dairy business and sent his milk to the creamery at Camden, from which the wholesale dealer in New York received his supply. Dairyman X., himself, furnished no milk directly to the creamery, but supplied the village. It was ascertained, however, that whenever he returned from his route to his farm he left the milk that was left over from the trip, with his son-in-law, who included this in his supply to the creamery. Milk had thus been received from farm X. during the month preceding the onset of the city cases, and there is practically no doubt that this constituted the chain of infection.

In commenting on this outbreak Bolduan points out the

great danger of having a bacillus carrier on a dairy, even when the individual, as in the present instance, was cleanly himself and kept his home and dairy much cleaner than the average dairyman.

A very interesting outbreak of typhoid fever on shipboard, due to a carrier, is related by Sawyer,⁴² which illustrates that a carrier may be of great danger to others even when not occupied in the preparation or handling of food. In this instance 26 cases of the disease developed within three and a half years on a ship carrying 21 men, and were all traced to one carrier. The vessel in question was a lumber steamer, and its relation to the appearance of typhoid among members of the crew was so well known to sailors that the ship was called the fever ship, and it was difficult to secure desirable men for its crew. On investigation the conclusion was reached, through a process of elimination, that the series of cases of typhoid fever among the crew arose from a focus on board the ship itself. The evidence finally tended to indicate that a certain member of the crew was a carrier. The serum of this man gave a positive Widal reaction and the typhoid bacillus was isolated from his stools. The man himself had had typhoid fever four years previously; he had nothing whatever to do with the handling of the food, but had evidently infected the others through the use of a common dipper which was employed by the crew in procuring water from an open cask which was kept on deck.

Sawyer remarks in conclusion that if the staff of the hospital at which the man had been treated for his typhoid had discovered the bacillus in his stools at the time of his discharge the other 26 cases with 4 deaths might not have occurred.

Pus Carriers.—While the majority of typhoid carriers are fecal carriers or urinary carriers, or both at the same time, it should be borne in mind, when investigating an outbreak of the disease, that still other possibilities exist. An instructive instance has thus been reported by Bigelow.⁴³ In this case a house epidemic was traced to an individual who had had an attack of typhoid fever some months previously, followed

by necrosis and abscess formation about the sternum. At the time of the investigation his blood gave a positive Widal reaction, while the urine and feces were found free from typhoid bacilli on three different examinations. In the pus which was obtained from two small sinuses communicating with the sternum, the organisms in question were, however, obtained on every occasion. The infection of the other members of the household had apparently taken place through fruit which the carrier had gathered some days before the onset of their attacks.

The Recognition of Typhoid Carriers.—The recognition of typhoid carriers of the fecal type is facilitated by the fact that the blood serum of such individuals usually gives the *Widal reaction*; exceptions occur, but they are relatively rare. The discovery of this fact throws a new light upon the significance of a positive Widal reaction persisting for many years following an attack. Formerly it was thought that such an occurrence was a normal event, but in view of our present knowledge it would be well to regard all such individuals as possible carriers unless the contrary can be proved. For reasons already indicated, special attention should be directed to females who give a history of typhoid fever, and especially so if symptoms pointing to disease of the gall-bladder exist or have existed in the past. Not too much reliance should be placed upon negative answers on the part of individuals, however, as carriers who know themselves to be such may purposely attempt to mislead the examiner.

Having thus picked the suspects the next step is to examine their feces as well as the urine. So far as the latter is concerned it is well to bear in mind that typhoid bacilli may be present in a perfectly clear urine (Frosch, v. Drigalski, Conradi) and that a specimen should accordingly not be reported as negative merely because it is not turbid. Preceding the collection of the fecal sample it has been recommended to increase the flow of bile by the administration of cholagogues, followed by a mild laxative (3 to 5 grams of inspissated ox bile per diem, for several days), with the view

of washing the organisms into the intestinal tract and thus facilitating their finding. This will frequently not be necessary nor practical, but the procedure may be resorted to in special cases. Care, of course, should be exercised to insure that the specimens submitted for examination actually come from the corresponding individuals.

Bacteriological Technic.—For the demonstration of typhoid bacilli in the feces a large number of cultural methods are available. Those most frequently employed are the methods of v. Drigalski-Conradi, of Endo, of Krumwiede and of Russel. It should be remembered, however, that the majority of these methods merely permit a differentiation of the typhoid from the colon bacillus, and not from the so-called intermediates, nor from the dysentery bacillus. It is hence necessary to identify colonies which are manifestly not due to the colon bacillus by further cultural methods, notably their behavior toward carbohydrate bouillons and litmus milk and their response to treatment with corresponding immune sera in high dilution.

From a practical standpoint, of course, the differentiation of the typhoid bacillus from the intermediates is not particularly important, since what has been said in the foregoing pages regarding typhoid fever in connection with the carrier question is equally true of paratyphoid.

In this connection it is well to emphasize the fact that more stress should be laid upon the cultural characteristics of suspicious colonies than upon their immediate reaction to antityphoid sera, bearing in mind that freshly isolated cultures not infrequently show a considerable degree of resistance to the action of agglutinins, which is lost, however, after a series of transplantations, when their behavior becomes typical of the usual laboratory strains.

A description of the more important methods for the isolation of the organisms follows:

The Drigalski-Conradi Method.—The medium is essentially a feebly alkaline, lactose meat infusion agar, to which litmus and crystal violet have been added—the latter to inhibit the growth of various organisms that may be associated with the

typhoid and colon bacillus in the feces, the former to distinguish between organisms that ferment lactose with acid production (colon bacillus) and those that do not (typhoid bacillus).

Preparation of the Medium.—The meat infusion agar is prepared in the usual manner. It should contain 10 grams of peptone, an equal quantity of nutrose,* 5 grams of salt and 35 grams of agar to the liter, the infusion itself being made from a pound and a half of lean beef or veal. The reaction is made neutral or feebly alkaline to litmus.

To a liter of the hot agar solution are added 130 c.c. of hot litmus-lactose solution, prepared as described below: the reaction is again tested with litmus paper and readjusted to a weak alkaline, after which the mixture is further treated with 2 c.c. of a hot sterile 10 per cent. solution of sodium carbonate and 10 c.c. of a freshly prepared 0.1 per cent. solution of crystal violet B in sterile distilled water.

The litmus solution advocated by Drigalski and Conradi was that originally recommended by Kubel and Tiemann and sold under their name. In its place any sensitive aqueous solution of litmus may, however, be used. 130 c.c. are boiled for about ten minutes, then treated with 15 grams of chemically pure lactose and boiled for fifteen minutes longer. If a sediment has formed, the supernatant fluid is decanted and the clear solution then added to the hot agar solution, as described. The final product may be kept in 100 or 200 c.c. lots until needed or it may be plated at once. The Petri dishes should be as large as possible (15 to 20 cm. in diameter) and covered to a depth of at least 2 mm. with the medium. The covers are not replaced until the steam has evaporated and the agar is quite firm. Contamination by organisms of the air does not occur, owing to the inhibitory action of the crystal violet.

* In lieu of the German product which is now not available, a substitute may be employed which is composed of 94 parts of peanut flour, 5 parts of casein and 1 part of sodium carbonate (Wallis, R. L. M., Indian Jour. Med. Res. Calcutta, April, 1917).

The *examination of the feces* is then conducted as follows: A small amount of the material in question—a bit the size of a split pea—is emulsified in about 10 c.c. of sterile saline or broth and a platinum loopful transferred to one of the plates. Here it is spread out over the entire surface by the aid of a sterile glass rod or a capillary pipette that has been sealed and bent to an appropriate angle.

Each plate is properly labelled and then placed in the incubator at 37° to 40° C. for twenty-four hours. At the end of that time it is examined with a hand lens for the presence of small transparent blue colonies. The colon colonies are large, red and opaque.

Suspicious colonies are fished, transferred to other media and tested in reference to their behavior toward an actively agglutinating antityphoid serum. A preliminary test in this direction may be conveniently conducted as follows:

Preliminary agglutination test (macroscopic slide agglutination method). A slide is charged with tiny droplets (large platinum loopfuls) of a 1 to 100 dilution of an actively agglutinating antityphoid, antiparatyphoid A and B, and anti-dysentery serum, placed in a row, together with a corresponding set of saline droplets for control. A tiny bit of the suspected colony is now emulsified, first in the saline, and then in the corresponding serum droplets. Agglutination will occur in the homologous serum within two or three minutes, and may be observed directly with the naked eye.

This method is very satisfactory and is now extensively employed in board of health and military hospital laboratories.

Should a positive reaction be obtained the test may be repeated with a pure culture and in various dilutions, the organism being further studied in reference to its fermentative properties* and its behavior, when grown in litmus milk. The table on page 94 will show the essential differences which exist between the most important representatives of the colon-typhoid-dysentery group.

* For this purpose the Hiss serum-water media are especially to be recommended (which see).

TYPHOID FEVER

	Litmus milk.		Fermentation.			
	Coagulation.	Acid production.	Dextrose.	Lactose.	Saccharose.	Mannite.
<i>B. typhosus</i>	0	± → alkaline	g = 0 a = +; g + a = 0; g + a = 0; g = 0	g + a = 0; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. paratyphosus</i> —A	0	+	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. paratyphosus</i> —B	0	± → alkaline	g = 0 a = +; g + a = 0; g + a = 0; g = 0	g + a = 0; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = 0
<i>B. coli communis</i>	+	+	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. coli communior</i>	+	+	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. proteus</i> (group)	+	±	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. dysenteriae</i> —Shiga	0	± → alkaline	g = 0 a = +; g + a = 0; g + a = 0; g = 0	g + a = 0; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = 0
<i>B. dysenteriae</i> —Flexner	0	± → alkaline	g = 0 a = +; g + a = 0; g + a = 0; g = 0	g + a = 0; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. dysenteriae</i> —Hiss—Russell	0	± → alkaline	g = 0 a = +; g + a = 0; g + a = 0; g = 0	g + a = 0; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = 0
<i>B. fecalis alkaligenes</i>	0	0	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. lactis aërogenes</i>	+	+	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +
<i>B. acidi lactici</i>	+	+	g + a = +; g + a = 0; g + a = 0; g = 0	g + a = +; g + a = 0; g + a = 0; g = 0	g = 0; g = 0	a = +

g = gas formation.

a = acid formation.

± → alkaline = primary acidity followed by alkali formation.

To differentiate between the typhoid, paratyphoid, colon and dysentery bacilli, Russell's double sugar agar will also be found very convenient (see below).

The Endo Method.—The medium in question is an ordinary neutral or faintly alkaline* 3 per cent. agar to which is added, *just before use*, 1 per cent. of lactose, and a solution of basic fuchsin that has been decolorized with sodium sulphite. On this medium typhoid and paratyphoid colonies appear colorless, while colon colonies, owing to the formation of aldehydes, are red.

The agar is kept on hand in flasks containing 100 or 200 c.c. each. When it is desired to use the medium the agar is melted, and, while hot, treated with 1 gram of chemically pure lactose and 1 c.c. of the decolorized fuchsin solution, per 100 c.c. The latter must always be freshly prepared, to which end 10 c.c. of a 10 per cent. aqueous solution of sodium sulphite are treated with 1 c.c. of a 10 per cent. solution of basic fuchsin in ordinary ethyl alcohol. (The proportions may vary a little with different lots of sodium sulphite and must be tried out, the point being to obtain a solution that is just decolorized.)†

When the decolorized fuchsin solution is added to the hot agar a certain amount of color returns but fades again on cooling, leaving the medium either a faint pink or altogether colorless. Large plates should be poured at once—to a depth of at least 2 mm.—and allowed to cool, with the covers off. When the agar has hardened the plates are inoculated with a tiny droplet of the fecal emulsion (a bit of fecal matter the size of a split pea to 10 c.c. of saline), which is spread over the surface with a sterile glass rod or a capillary pipette that has been sealed and bent to a convenient angle. They are incubated at 37° to 40° C. and examined on the following day. Suspicious-looking colonies are then fished and tested against an actively agglutinating serum by the macro-

* To litmus.

† Teague has pointed out that a solution of the sulphite that has been heated for twenty minutes at 15 pounds' pressure and layered with petroleum to the extent of about 1 cm. will keep for three weeks or longer.—*Jour. Am. Med. Assn.*, 1918, vol. lxx, p. 454.

scopic slide method, as described above, after which they may be further studied as indicated.

Krumwiede's Method.—The medium employed is a 1.5 per cent. beef extract (0.3 per cent.) agar, which is made just alkaline to litmus and kept on hand in 100 c.c. lots. When needed, 1 per cent. of lactose and 0.1 per cent. of glucose is added to each flask together with a certain quantity of brilliant green, and 1 per cent. of Andrade's indicator, after which the mixture is brought to the neutral point of the indicator by the addition of acid. The principle underlying the method is the fact that the brilliant green not only inhibits the growth of all Gram-positive and many Gram-negative bacteria, but in certain dilutions also shows a differential action upon members of the typhoid-colon group. To this end two plates are always prepared in each case, of which one corresponds to a dilution of 1 to 500,000 and the other to one of 1 to 330,000. The paratyphoids and the *Bacillus lactis aërogenes* are not affected by either dilution; the typhoid is restrained by the lower dilution only, while the growth of the dysentery bacillus and other members of the colon group is inhibited.

When the plate is viewed at an angle against a dark background the typhoid and paratyphoid B colonies appear with serrated edges and snowy white, or at most tinged a faint pink, owing to fermentation of the glucose, while the acid producers are red in consequence of the return of the fuchsin color base to the dye itself.

Krumwiede insists that the particular specimen of brilliant green that is available must first be tried out to ascertain the exact dilution which will effect the differentiation of the typhoid from the colon and dysentery groups. The agar must be perfectly clear and of the requisite reaction. His instructions for the preparation of the medium follow:*

When needed the stock agar (see above) is melted and each bottle treated with 1 per cent. of Andrade's indicator, when acid (n HCl) is added to bring the mixture to the neutral point. The indicator is prepared as follows: 100 c.c. of a

* Taken from Hiss and Zinsser's Bacteriology, Appleton & Co., 3d edition, 1916, p. 136.

0.5 per cent. aqueous solution of *acid* fuchsin are treated with 16 c.c. of normal sodium hydrate solution, when in the course of about two hours the dye is reduced to the color base. If the agar has the proper reaction—and this is of the utmost importance—*i. e.*, if it is neutral to Andrade, the color is deep red while hot, but fades completely on cooling. In order to determine this it is recommended to pour a few cubic centimeters of the acidified hot agar into a test-tube and to cool this under the tap, when the reaction is finally adjusted by adding more acid or alkali, as the case may be. The neutral point of Andrade's indicator corresponds to an acidity of 0.6 to 0.7 per cent. (normal hydrochloric acid) in terms of phenolphthalein.

The requisite amount of lactose and glucose are conveniently added from a sterile stock solution of the two sugars—containing 20 per cent. of the former and 2 per cent. of the latter respectively; 5 c.c. of this solution represent the requisite quantity for 100 c.c. of the agar.

To prepare the brilliant green solution 0.1 gram of the dye is accurately weighed on a foil, washed with boiling water into a 100 c.c. volumetric flask and made up to the mark when cool. The flask should be clean and neutral (by test). Fresh solutions vary in activity; they keep about one month.

Different lots of agar with the same dye solution act uniformly; a new batch or a new solution must be tested.

Any variation in the composition of the medium necessitates a readjustment of the dye concentration; this statement cannot be overemphasized.

As I have stated above, two dilutions of the dye are used, and to this end 0.2 c.c. of the stock solution is added to one lot of 100 c.c. of agar (giving a dilution of 1 to 500,000) and 0.3 c.c. to another (giving a dilution of 1 to 330,000).

Each bottle of 100 c.c. is finally poured into six plates, which are then left uncovered until the agar has solidified. Porous tops are used in order to secure dry plates and prevent diffusion. To this end a piece of filter paper is placed in the cover of each plate.

Duplicate sets—corresponding to the two solutions of the dye—are inoculated as above, incubated as usual and exam-

ined the following day. Suspicious-looking colonies are then fished and tested as described.

From the description given it is clear that satisfactory results will only be obtained with this method if the medium is prepared exactly as indicated, and to judge from personal experience even then results will not always be just as desired. Kligler has recently recommended the substitution of 0.25 c.c. of a 1 per cent. aqueous solution of neutral red per 100 c.c. of the medium in the place of the Andrade indicator, and states that he has found this more useful, as it gives a color differentiation which is lacking with the original method, the typhoid bacillus leaving the color unchanged.

Russell's Double Sugar Medium.—The medium in question is a 3 per cent. beef extract agar, which is at first made 0.8 per cent. acid to phenolphthalein and subsequently brought to the neutral point for litmus, a 5 per cent. aqueous solution of the latter having previously been added in a quantity sufficient to render the medium a distinct purple. This is further treated with 1 per cent. of lactose and 0.1 per cent. of glucose, which are added dissolved in a little hot water. The medium is then tubed and fractionally sterilized in an Arnold sterilizer—for fifteen minutes at a time. Before slanting Kligler* has suggested that each tube be further treated with sterile basic acetate of lead solution to the extent of 0.05 per cent. (0.5 c.c. of a 1 per cent. solution, per 10 c.c. of medium).

Suspicious colonies that have been isolated by any one of the plating methods described above are inoculated upon this medium (using the Kligler formula), both by streak and stab and incubated for twenty-four hours. The typhoid bacillus gives a colorless growth on a blue surface, while the end of the stab appears red; the medium along the line of the stab, moreover, shows a distinct browning. The paratyphoid B shows the same features as the typhoid, but produces gas bubbles in addition. The dysentery bacilli grow like the typhoids, but produce no browning. Paratyphoid A likewise

* Kligler, I. J.: Modifications of culture media used in the isolation and differentiation of typhoid, dysentery and allied bacilli, *Abst. of Bact.*, 1918, vol. ii, p. 18.

does not produce a brown color but forms gas and acid at the bottom of the stab, while the surface remains blue. The colon bacillus finally produces acid and bubbles throughout.

The Management of Typhoid Carriers.—*Medical Treatment.*—When the significance of the typhoid carrier was first realized numerous attempts were made to destroy the typhoid bacilli in the intestinal canal by disinfectants. As was to be expected, in view of what we now know regarding the origin of the organisms, the results were absolutely *nil* so far as any permanent effect was concerned.

It was then suggested that it might be possible to wash the gall-bladder free from organisms by the use of cholagogues (inspissated ox gall, bile salts). The flow of bile is thus increased, it is true, and bacilli enter the intestinal canal in increased numbers, but it was found that even after the administration of 3 to 5 grams of inspissated bile a day, continued for a period of three or four months, the bacilli did not disappear. It was noted their number diminished and that there were even periods during which they disappeared, but in the end they always returned. That this should be so is, of course, not surprising, if we remember the anatomical relations of the gall-bladder to the common duct and the mechanical difficulties which stand in the way of any attempt to "wash out" the gall-bladder by means of the natural secretion of the liver. But even if this were possible we could not expect to "wash out" those organisms which in some manner have found their way into the ducts of the numerous glands and thus into the walls of the gall-bladder, and which would serve as a small but constant reserve. The problem hence resolves itself into the question of either killing the organisms in their stronghold by chemical or biological methods or of removing the stronghold itself. All attempts in the former direction have thus far led to nothing,* and I would particularly emphasize the uselessness of vaccines to this end.

* Lentz⁶ reports that during the administration of fortoin (formalinized cotoin), given either by itself, but especially in combination with extract of phytolacca (laxative and cholagogue) and bicarbonate of soda (alkali) the elimination of bacilli diminished and even ceased for days at a time, and he accordingly suggests that some formalin product may in the end be shown to produce the desired result.

Whether or not anything can be done *during the course of the disease* to prevent the development of the carrier condition seems doubtful at present, but in those cases in which infection of the urine has taken place, it would seem that much good can be accomplished by the administration of hexamethylenetetramin (urotropin).

Some writers, such as Semple and Greig,⁴⁴ however, claim that permanent sterilization of the urine cannot be accomplished in this manner. It is to be noted, however, that at the time when this view was expressed the drug was given in very small doses. Crowe,⁴⁵ in 1917, emphasized its value in typhoid bacilluria and pointed out that providing large doses be given—at least 75 grams per diem—the drug appears in the gall-bladder even in a concentration which suffices to render the bile an unsuitable medium for the growth of bacteria.

Surgical Treatment.—There remains then for consideration the question of surgical interference, and so far as the evidence goes this method is the only one that has thus far led to satisfactory results. In 1907 Dehler³⁵ reported two successful cholecystotomies in the case of chronic typhoid carriers, occurring in an insane asylum under his charge.* In 1912 he³⁵ referred to two additional cases with a similarly satisfactory outcome. In both active gall-bladder symptoms had existed, and in themselves warranted the operation irrespective of the carrier condition. Subsequent investigations, however, have shown that such a favorable outcome does not always occur, and the later tendency has been to perform cholecystectomy rather than cholecystotomy. This seems more reasonable since we know that the bacilli are found not only in the contents of the gall-bladder, but in its walls as well.

Quarantine and Control of Carriers.—But while operative treatment may be urged upon every fecal carrier, and may be accepted by those who actually suffer from gall-bladder symptoms, and even by some of those who are personally not inconvenienced by their condition, but wish to be cured

* According to Frosch the result in these two cases was not a permanent one,

from altruistic motives, it is clear that the vast majority of the cases will not come to operation of their own free will, nor can they be compelled to subject themselves to the dangers incidental to such treatment. The problem then is manifestly to subject the chronic carrier to such supervision and regulation as to render him as little dangerous to others as possible. *To this end it is essential that no case of typhoid fever, and the same is true of paratyphoid, should be discharged from medical supervision until his status in reference to the carrier condition has been determined by the proper authorities.* It has accordingly been suggested that every typhoid convalescent be regarded as a carrier until five successive examinations of both urine and feces, at intervals of three days, have given negative results, and until any other focus of infection that has developed in the course of the malady (discharging sinuses, otitis media) has been cured or shown to be free from typhoid bacilli. This work should be under the direct supervision of the health department, but could be carried on very well, in the case of hospital patients, by the department of clinical pathology. Should the patient be discharged from the hospital while still in the carrier stage, proper notification should be made to the health department, which should then assume control.

While the supervision of temporary carriers should offer relatively little difficulty, the *problem of the chronic carrier* is a very formidable one. As I have pointed out before, there is reason to believe that in a city of the size of New York there may be 25,000 carriers, and to prevent any one of these from conveying the infection to others would indeed be a colossal undertaking. It is a problem which nevertheless seems capable of partial solution at any rate, if we bear in mind that the typhoid carrier is dangerous to others largely through his contact with foodstuffs. Evidently those carriers are the most dangerous who are themselves unaware of their condition, and the manifest duty of the authorities is to explain this danger to such people. A great deal of valuable coöperation could, no doubt, be secured in this manner, which in itself would bring about an improvement. It is clear, however, that without a certain degree of police regulation on

the part of the health department, education of the carriers alone would not produce the desired result. Regulation is evidently the *sine qua non* of public safety. To this end *all carriers should be registered* as soon as their condition has been recognized and the authorities notified of any change of address or of occupation. This should be verified from time to time and the records thus kept up to date. Next in order should come such legislation as would bar every carrier from engaging in any occupation which would bring the individual into contact with public food supplies. The most superficial study of the problem shows that in the majority of cases of typhoid fever which have been traced to carriers the latter were found to be engaged in some branch of the dairy business or as cooks. Such legislation could be supplemented by the demand that no individual engaged in the handling of public foodstuffs be permitted to engage help without a permit from the health authorities stating that the individual is not a carrier. Still further legislation would, of course, suggest itself as desirable, but ordinances covering the three points just considered, if enforced, would go far to eradicate typhoid fever from those cities and towns, at any rate, in which an adequate sewerage system and a safe drinking water supply already exist. Where this is not the case the danger from the carrier is, of course, proportionately greater, and in handling the situation it would appear simpler to eliminate the existing deficiencies than to attempt to regulate the disinfection of the carriers' discharges which would be the only alternative.

In country districts, in which wells represent the only supply of drinking water and in which the backyard privy is only too often unpleasantly close to the former, the menace of the carrier is indeed great, and becomes even more formidable when, as frequently found, the food supplies and the household dairy are, of necessity, in the hands of the same individual, who herself more than likely is unaware of her fatal gift. Education coupled with *prophylactic vaccination* of all those who are thrown in contact with the carrier will here, no doubt, accomplish a great deal of good. The *sine qua non*, of course, is here also the recognition of the carrier,

and to this end we require the coöperation of the attending physician and the local health officer. Without such assistance no progress can be made, and in its absence we shall only too often find the disease dragging on in a community for years and years, until the majority of the individuals who have been thrown in contact with the carrier have finally acquired an immunity through an attack of the malady.

In fine, it should be borne in mind that while *vaccination* does not rid the carrier of his organisms, the number of would-be-carriers will be diminished in direct ratio to the extent to which vaccination of all those who in any way may be subjected to the possibility of becoming infected, is practiced. In other words, there is a theoretical possibility of stamping out typhoid fever through universal vaccination, irrespective of the problem presented by the typhoid carrier. This has been well shown in the course of the present war, where typhoid fever is as uncommon as formerly it was one of the principal scourges of military camps.

PARATYPHOID FEVER.

While we have less specific information relating to the role of carriers in the dissemination of paratyphoid fever than in connection with typhoid fever, there is sufficient evidence to show that this is practically the same, in so far at least as infection with the paratyphoid B bacillus is concerned. Here also the organism has been found to invade the gall-bladder; here also does it appear in the feces, not only during the active stage of the malady, but in a certain percentage of cases also during convalescence. Passive carriers of the organism further are known to occur, and in certain districts are indeed so common, that it is exceptional to meet with individuals who are not carriers; and that the disease may assume epidemic proportions has been abundantly demonstrated—as with us during the recent concentration of our army on the Mexican border.

For practical purposes, therefore, it is unnecessary to consider paratyphoid carriers separately from typhoid carriers. Their import, their recognition and management are essen-

tially those of the latter, and have been in a large measure considered under that heading, so that a recapitulation at this place is scarcely necessary.

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EPIDEMIC CEREBROSPINAL MENINGITIS.

THE recognition of the manner in which the dissemination of epidemic cerebrospinal meningitis takes place is largely due to the painstaking investigations of von Lingelsheim¹ during the epidemic which prevailed in upper Silesia during 1904 and 1905, in the course of which he could show that the organism in question may be demonstrated in the nasopharynx of practically every patient. A number of previous investigators, it is true, had claimed that the meningococcus may be found in the secretions of the nose, but barring the isolated observations of Kiefer² in 1896 and of Albrecht and Ghon³ in 1901 it is doubtful whether any of the others had actually been dealing with the meningococcus. A superficial analysis of Lingelsheim's initial series of 787 examinations of the nasal and pharyngeal secretions of meningitis cases shows that a positive result was obtained in only 182, *i. e.*, 23.12 per cent. But on classifying these cases in accordance with the distance from which the material was sent, the percentage of positive findings is increased to 33 per cent. in the case of those in which the examination could be conducted on the same day as the collection of the specimens. It is noteworthy furthermore that of the 130 positive results of this series (corresponding to 390 cases) 104 were obtained in patients whose illness had not yet extended beyond the fifth day, which gives a percentage of 66.6. Between the sixth and the tenth day the positive findings represented 24.56 per cent.; between the eleventh and the twentieth days 11.29 per cent., and later than this date 4.39 per cent. Including all positive findings, irrespective of their geographical origin, *i. e.*, 182 cases, 147, *i. e.*, 80.07 per cent., had not passed beyond the fifth day of the disease.

v. Lingelsheim further showed that great care is necessary in the collection of the specimen and that material from the anterior and middle nares always furnished a negative result.

Eliminating such sources of error, in addition to those arising from delay in the examination, as well as all cases which had passed the fifth day of the disease, he finally obtained a series of 49 cases, in 46, *i. e.*, in 93.8 per cent., of which the meningococcus could be isolated.

These findings are, of course, of the greatest importance, for they indicate on the one hand, the *habitat of the organisms* from which a transference to other individuals can readily take place, and they have opened up avenues for the investigation of the broader epidemiological aspects of the malady which formerly were closed.

Regarding the route by which the organism reaches the meninges there is some difference of opinion. Some observers believe that infection takes place directly through the lymph channels penetrating the cribriform plate of the ethmoid, while others have expressed the opinion that a general septicemia precedes the meningitis proper. However that may be, there can be no doubt that the nasopharynx is the portal of entry, and that the disease may be conveyed to others through the nasopharyngeal secretion in connection with the act of coughing, of sneezing or through the sputum spray during ordinary conversation.

The question now arises whether the disease can be transmitted only during the active period of the malady, or whether the organisms may persist sufficiently long as to warrant the conclusion that there are convalescent meningitis carriers; and further, whether, as in the infections previously considered there are healthy carriers, who without having developed the disease proper, have yet become infected through contact with patients or other carriers and are themselves capable of conveying the disease to others.

Active Carriers.—It has already been pointed out that whereas the organism can be demonstrated in the nasopharynx of practically every case during the first five days of the malady, the percentage of positive findings rapidly diminishes thereafter, so that as in V. Lingelsheim's series, following the twentieth day the figure dropped to 4.39 per cent. V. Lingelsheim also mentions that, whereas in early cases the organisms were obtained in large numbers and in almost pure

culture, this picture changed after a few days, other organisms, notably the catarrhal micrococcus and pneumococci replacing the meningococcus. In a few series of abortive cases in which an abundant herpetic eruption represented the principal clinical symptom, the organisms already disappeared after twenty-four hours. Any growth that was obtained after the expiration of the third week of the disease was usually meager and developed only after forty-eight hours' incubation. When once the cultures had become negative they usually remained so. But occasionally there was an exception. In one of the cases (51) a positive result was thus obtained on March 23; on March 27 and 31, as well as on April 6 and 14, the cultures were negative, but positive again on April 18 and 25. In this case there had thus been a negative interval lasting approximately three weeks, which was followed by a return of the organisms. In another case (141) the malady began on February 26. The throat cultures were negative from March 9 to April 6, when a positive result was obtained for the first time.

From v. Lingelsheim's table it is indeed impossible to draw any very definite conclusions regarding the frequency with which the organisms persist beyond the twenty-first day, as the number of examinations covering this point is too small. His own conclusion that 4.39 indicates the percentage of positive findings after the expiration of the third week *may* be correct, but it is scarcely warrantable on the basis of the limited number of consecutive examinations which he has reported in connection with individual cases. That the organisms *may* persist for a long period of time is clearly indicated by his findings in one case, in which isolated colonies could yet be obtained at the expiration of three months from the beginning of the malady. Such cases, however, are unquestionably rare, and practically speaking we may say that *only a very small percentage of individuals who have presented the classical picture of meningitis harbor the organism long enough during convalescence to be classed as carriers.*

While the active meningitis patient may be dangerous to his immediate entourage, it is after all rare that he conveys the disease to others. Even if he could do so he would not be in a

position to directly infect many people. He is after all sick in bed while the malady lasts, and by the time that he is again able to go out his organisms have usually disappeared. He nevertheless represents a very formidable menace to the community at large, through the readiness with which he is able to produce carriers among those with whom he is brought into contact, even though these do not necessarily or even usually develop the disease themselves. The danger lies in the fact that these *passive carriers* may in turn give rise to a new series of carriers and so on indefinitely. Since the liability to the development of the actual disease is after all relatively limited, it may happen that at the outset of an epidemic the number of active cases is quite small, but that a large number of passive carriers is being rapidly produced through which susceptible individuals are then promptly reached.

Passive Carriers.—Regarding the liability to passive infection, on the part of a patient's attendants, it is clear from the available data that this may be very considerable. As a result of his investigations v. Lingelsheim arrived at the conclusion that from 10 to 15 per cent. of a patient's entourage—comprising attendants, members of the family and near friends—is transformed into carriers. This is evidently too conservative an estimate, for other observers, as well as he himself, subsequently obtained much higher values. He thus mentions in his collective report of 1908, that in connection with 6 cases, where he had occasion to make a careful study of the other members of the patient's families, he invariably found all of them infected.⁴ Ostermann⁵ reports positive findings in 17 individuals out of 24 who had come in contact with active cases. Dieudonné and Hasslauer⁶ found nine roommates of a diseased soldier infected. Particularly instructive also are the findings of Bochalli.⁷ This investigator examined an entire battalion of 485 soldiers, among whom a case of the disease had appeared, and discovered 42 carriers. Of the sixteen roommates of the patient ten, *i. e.*, 62.5 per cent., were carriers. Thirteen additional carriers belonged to the patient's company. Flack,¹⁷ on the other hand, in reporting on cerebrospinal fever in the London district

from December, 1915 to July, 1916, mentions that of 1629 contacts of 60 cases of the disease, only 139, *i. e.*, 8.53 per cent., were found to be carriers.

From the available data it is very difficult to draw any definite conclusions regarding the ratio between the percentage of patients and healthy carriers. This must of necessity vary considerably. In those cases in which there is much irritation of the upper respiratory tract leading to a great deal of coughing and hawking the chances for a wide dissemination of the organisms are, of course, much greater than otherwise. So much is certain in any event that for every patient there is a very considerable number of carriers who have developed in the proximity of the patient, and as they in turn can give rise to other carriers and these to still others, the total number existing at the height, or more likely during the ascending period of an epidemic must be very large.* Being healthy carriers, *i. e.*, individuals who are unrestricted in their movements, the disease will naturally not remain local, but become disseminated over an unlimited territory, so long, at any rate, as proper quarantine regulations do not exist or cannot be enforced. In this manner the various epidemics of the disease are readily explained. The pandemic which started in Europe in 1904 and spread over the entire globe within the following five or six years has not died out yet, either in Europe or in our own country, and has recently become a grave menace in our military camps, necessitating most active and vigorous methods to prevent its assuming renewed epidemic proportions. As yet no official information is available to indicate the ratio between patients and carriers in our cantonments but so far as I have been able to learn the experience gathered thus far corresponds to that obtained by the earlier investigators referred to above.

Duration of the Carrier Stage in Passive Carriers.—As regards the duration of the carrier stage in healthy individuals, the available data show the following: In Bochalli's series of 29 carriers the organisms had disappeared at the expiration of seven days in 9, after two weeks in 12, and

* Flack reports that of 275 non-contacts which he examined, 6, or 2.18 per cent., gave a positive result.

after three weeks in 6, while in 2 they remained for four weeks. The findings obtained by Flack in 185 carriers are shown in the following table:

	Contact carriers.	Per cent.	Non-contact carriers.	Per cent.
Under 2 weeks . . .	20	16.12	12	19.67
2 to 4 weeks . . .	45	36.29	32	52.46
4 to 6 weeks . . .	26	20.97	5	8.19
6 to 8 weeks . . .	14	11.29	2	3.28
8 to 10 weeks . . .	4	3.23	7	11.48
10 to 12 weeks . . .	5	4.03		
Over 12 weeks . . .	10	8.07	3	4.92

It would thus appear that the duration is about the same in this type of carriers as in those who have passed through an attack of the disease.

Virulence of the Organisms.—From the very common occurrence of healthy meningococcus carriers during an epidemic of the disease it might be argued that the organisms which were regarded as meningococci in the individuals in question were in reality no true meningococci, or possibly strains only of non-virulent character. There is nothing to support such a view, however, and all the facts are against such a possibility. It has thus been conclusively shown that in individuals who have in no way been exposed to meningitis either directly or indirectly, as far as could be ascertained, meningococci are rarely demonstrable in either the throat or nose. That they should be found in isolated instances can, of course, not be surprising, if we bear in mind that the organism is not known to occur outside of the body of man, in nature, and that so long as the disease has not died out altogether in a given district, there must still remain a few persons in which the organisms persist. The rapid increase in the number of carriers as an epidemic develops, coupled with the relatively brief duration of the carrier stage, clearly suggests that their presence is not immaterial. Direct investigations furthermore, and notably inoculations of monkeys, have shown conclusively that there is no difference in the virulence of the organisms obtained from healthy carriers, as compared with those derived from actual cases of meningitis. And last but not least is the direct evidence connecting outbreaks of the disease in a community with the introduction of carriers

coming from infected districts. Concrete examples of such outbreaks are given below.

Habitat of the Organisms.—As regards the manner in which an individual becomes a carrier and more particularly of the predisposing causes very little is known. The fact that the organism's resistance outside of the body is so very slight suggests, of course, that in the human nasopharynx it must find special conditions favoring its growth. Bearing in mind the common occurrence of catarrhal conditions associated with lymphatic involvement in civilized races more particularly, one cannot help but think that the ready availability of certain serum constituents which are poured out upon the surface and which collect in the various nooks and corners of the mucous membrane of the nasopharynx may prove to be the point of attraction. Some writers lay stress upon an increased secretion of mucus as a factor favoring the development of the organisms in the throat, but it seems more likely that the underlying inflammatory process with the resultant exudation of serum is the more important. Unfortunately no systematic bacteriological examinations of the lymphatic structures of the throat have thus far been made in carriers, but we may logically assume that the organisms do not develop to any special extent upon the exposed surfaces of the mucous membrane, but more likely in its depth, and particularly in the clefts of the larger lymphatic structures, such as the pharyngeal and faucial tonsils. In actual cases of meningitis, both acute and chronic, in children as well as in adults, Westenhoeffer⁸ invariably found a very considerable hypertrophy, hyperemia and hypersecretion of the pharyngeal tonsil, and both he and v. Lingelsheim, as well as Meyer,⁹ could demonstrate the meningococcus directly in the secretion taken from the depth of the recesses. Meyer, moreover, found them in the peripheral portion of the pharyngeal tonsil, while in the deeper parts they were lost. The faucial tonsils in contradistinction to the pharyngeal gland Westenhoeffer found less frequently involved.

Similar conditions no doubt exist in the carriers, though in these the pharyngeal tonsil cannot play the prominent role which Westenhoeffer has assigned to this structure in cases of the actual disease. According to Trautmann the pharyn-

geal tonsil usually disappears after the eighteenth year. In view of the fact that in adults the carrier state is decidedly common, whereas the malady itself has a special predilection for children in whom the gland is present, and whereas all adults contracting the disease showed the same hypertrophy as children, this observation would suggest that this structure may play an important role as portal of entry when it is developed, but that it is not essential as a nidus for the development of the organisms in carriers. In the latter the remaining lymphatic structures and mucous glands no doubt serve as points of anchorage for the organisms.

A careful study of *the distribution of meningococci in the upper respiratory tract* of carriers has been made by Herrold.¹⁵ This investigator examined 93 segregated men with the results presented in the following three tables:

TABLE I.—THE INCIDENCE OF POSITIVE CULTURES OF MENINGOCOCCI FROM DIFFERENT SOURCES OF THE UPPER RESPIRATORY TRACT OF NINETY-THREE CARRIERS.

Source of cultures.	Positive.	
	Number.	Per cent.
Nasopharynx	66	70.9
Tonsils	29	31.2
Anterior superior nares	16	17.2
Sputum	12	12.9

TABLE II.—SUMMARY OF RELATIONS OF POSITIVE CULTURES FROM ELSEWHERE THAN THE NASOPHARYNX.

	Number.
Positive tonsil, negative nasal and sputum cultures . . .	25
Positive nasal, negative tonsil and sputum cultures . . .	11
Positive sputum, negative nasal and tonsil cultures . . .	8
Positive tonsil and nasal, negative sputum cultures . . .	2
Positive tonsil and sputum, negative nasal cultures . . .	1
Positive nasal and sputum, negative tonsil cultures . . .	2
Positive tonsil, nasal and sputum cultures	1

TABLE III.—A COMPARISON OF THE PERSISTENCE OF THE CARRIER STATE ACCORDING TO THE DISTRIBUTION OF MENINGOCOCCI.

Type of carrier.	Number in each group.	Incidence of persistence after six weeks.	
		Number.	Per cent.
Positive nasopharynx and elsewhere . . .	39	28	73.0
Positive nasopharynx, negative elsewhere . . .	27	17	63.0
Negative nasopharynx, positive elsewhere . . .	11	6	54.6
Negative nasopharynx and elsewhere . . .	16	3	18.8

The results speak for themselves and warrant the conclusion that cultures should be taken not only from the nasopharynx but from the tonsils and anterior superior nares as well.

Practically important, further, according to Westenhoeffer; is the fact that in children median otitis frequently, in fact invariably, develops, and that in this situation the organisms may possibly persist for some time in some of the convalescent carriers.

Relative Insusceptibility to Meningitis.—The question why there should be such a discrepancy between the number of carriers and of cases of the actual disease may in part be explained upon the basis of the anatomical differences in the lymphatic structures of the nasopharynx just referred to. But it is also conceivable that the disparity is more apparent than real, and that adequate clinical and laboratory investigation might show that many of the supposedly healthy carriers are in reality at the time not in a condition of absolute health, and that many of the “insignificant or minor” acute catarrhal conditions which are observed in the course of an epidemic of meningitis, as well as at other times, may in the former instance be due to infection with the meningococcus. As a matter of fact it is well known that during epidemics of the disease many of the patient’s attendants and housemates, many of whom we now know to be carriers, develop an acute pharyngitis, while abortive cases with actual meningeal symptoms are common, the true nature of which under ordinary conditions would never have been recognized or even suspected. Viewed from this standpoint the occurrence of actual meningitis would merely represent a possible and more or less accidental incident in the course of a meningococcus infection, just as certain cases of lobar pneumonia can only be regarded as a more or less accidental occurrence in the course of a corresponding pneumococcus infection. In both types of infection the clinical picture may, on the one hand, be that of a simple pharyngitis, while on the other abortive lung, *sc.* meningeal symptoms may appear, and in yet others the orthodox symptoms of a malignant pneumonia or meningitis control the situation. But just as the milder pneumococcus infections are more common than the severer types, so

is it conceivable that mild meningococcus infections may be more common than is generally supposed.

However this may be, the carrier menace is the same, for from an epidemiological standpoint it would make very little difference whether a carrier is a healthy carrier or one convalescent from an infection so mild that it was not recognized, for the main danger in connection with the carrier is the individual's ignorance of his condition.

To illustrate the relatively low susceptibility to meningitis, in adults at least, it may be mentioned that according to Medlar,¹⁰ at Camp McClellan, the percentage of meningococcus carriers during the months of November and December, 1917, was between 3 and 6, but rose to from 12 to 20 in about 3000 cultures made, while the disease had in no sense assumed epidemic proportions, although there was an increase of the sporadic cases. In only one instance did more than one case of meningitis develop in a company, while the number of carriers was in some as high as forty. In this connection it is interesting to relate that synchronously with the increase in the number of carriers there developed an epidemic of sore throats. In at least half a dozen cases it was observed that men with severe pharyngitis showed on culture large numbers of meningococci,* and that these disappeared when the pharyngitis cleared up.

To what extent the individual carrier is a menace to others will, of course, depend very much upon circumstances, irrespective of the number of organisms that he may harbor in his throat. Other things being equal the latter factor will, of course, be a very important one. But it stands to reason that an individual harboring the organisms only in small numbers may be more dangerous than another who harbors many, if he be suffering from an irritative condition of the throat leading to much hawking and coughing, while the latter may be free from this and hence less liable to spray his surroundings. Then again much will depend upon the susceptibility of the people with whom the carrier comes in

* Two of these cases developed meningococcus meningitis a few days after their pharyngitis cleared up.

contact. If these be children or young adults and particularly if they come from a territory that has been free from meningitis the danger will be greater, even though the carrier's throat be but lightly infected. For with virgin soil, of the most susceptible material, available for infection, only the proverbial spark will be necessary to initiate a most extensive conflagration. The mildly infected carrier, even though he himself infect perhaps but a single susceptible individual, may thus start a chain which will end only when suitable soil is no longer available. It is for this reason that the introduction of a carrier among a body of troops which has previously been free from the disease, and particularly of men who have been brought together from hitherto immune districts, is so liable to call forth an outbreak of epidemic proportions which may be most difficult to control. Conversely it has been noted that the incidence of the disease in those military camps in which a systematic search for carriers is made and these are removed is smaller than in others where such precautions are not taken.¹⁷

Generally speaking, the more intimate the contact between the carrier and his victim, the greater the danger, and it is for this reason that a carrier mother will prove a particular menace to her children, and these in turn to each other. If we add to what we may call the normal danger arising from contact between carriers and the exposed the dangers incidental to living in close quarters, in badly lighted and ventilated rooms, especially during the winter and early spring seasons, with the resultant debilitating effects and the general tendency to "colds" and the resultant coughs, we may form a fairly clear idea of the consequences, particularly if, as I have said, the soil is virgin and the natural or acquired immunity negligible.

While the majority of observers lay stress upon the dissemination of the disease through infected particles of sputum, it should not be forgotten that freshly infected food material and infected dishes, napkins and the like, may possibly play a role as well. Much additional work remains to be done in this connection, and in the meantime it will be well to err on the side of extra precaution.

While the foregoing data leave no reasonable doubt that meningococcus meningitis is disseminated by carriers, it is rarely possible to connect individual carriers with individual patients bacteriologically, in such a manner as to definitely prove that infection took place through such and such a person and in no other way. Even when a carrier has been found in the household of a patient there still exists the possibility that the carrier was infected by the patient instead of *vice versa*. As only the occurrence of an actual case of the disease leads to an examination of the remaining members of a household we would rarely have previous knowledge of the bacteriological flora of the throats of the various people, and in the absence of such knowledge our chain of evidence would naturally be defective. Conditions here are very much the same as in a disease like cholera, where, as we have seen, the carrier may have left the locality which he has infected before the disease actually appears. A number of suggestive cases, however, have been reported in the literature, and a few of these are here related.

Examples of Carrier Activity.—An instructive situation has been reported by Flatten,¹¹ in which the evidence connecting the carrier with the patient is perhaps as clear as can be demanded under the circumstances.

At the time when the principal epidemic ravaging upper Silesia was centered at Königshütte and its vicinity, a secondary outbreak occurred in Vossowska and its surroundings, the relation of which latter points to each other, and the railroad is shown in the accompanying diagram. At Vossowska are located two saw mills, two foundries and a chemical factory, and, as indicated in the diagram, it is a junction of two railroads.

On March 15 and 16 two cases of meningitis developed among the children of two workmen of the chemical factory who resided at Klein- and Gross Stanisch, respectively—Anna W. and Albina Cz. In Anna's house there resided at the time a woman (X) who had visited relatives at Laura-hütte, from February 9 to 18, and who could very readily have become a carrier there. She had attended the funeral of a child that had died from meningitis and had brought

some of the clothing of the dead child with her. This she unpacked on March 14 or 15, *i. e.*, about a month after her return, in the presence of Albina.

Bearing in mind the low grade of vitality of the meningococcus, and particularly the fact that after remaining in the

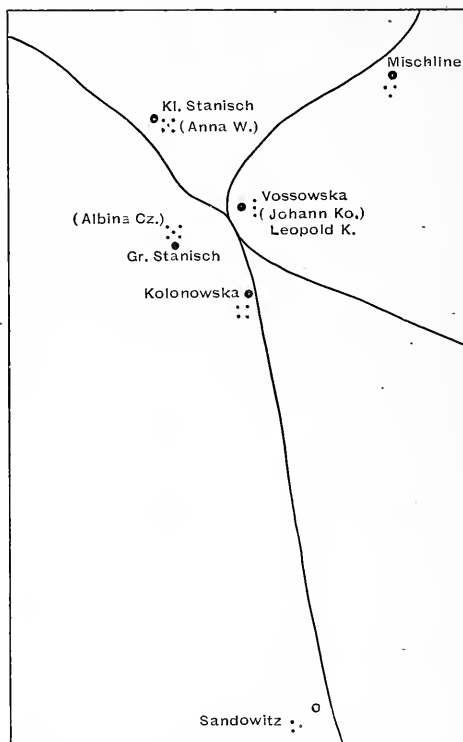


FIG. 1.

dried state for only twenty-four hours the organisms are dead, we can eliminate the unpacking of these clothes as a causative factor of the outbreak of the disease. This is practically ruled out, moreover, by the incubation period of the disease, which is very rarely shorter than 3 or 4 days. On the other hand we must remember that twenty-five days had

elapsed between this woman's return and the outbreak of the disease in Anna and Albina, and that she might very well have ceased to be a carrier at that time, but have given rise to another carrier. As a matter of fact, Flatten relates that meningococci were found in the nose of both Albina and the latter's mother—in the case of the mother on March 20. It is thus quite conceivable that she may have been the carrier who really infected Anna and Albina, while she in turn was infected by the woman X.

On March 16 another case of meningitis developed, the victim being Johann Ko, the son of a workman in one of the foundries of Vossowska, and residing there. This man's stepdaughter had been associating with Albina's family. On March 24 Leopold K., a cousin of Albina, was taken ill. On March 26 followed the case of Albina's brother.

On March 28 and 30 three children developed the disease in Mischline. Their father worked in one of the saw mills of Vossowska and was shown to be a meningococcus carrier; one brother worked in the chemical factory and a sister who was proved to be a carrier alongside of one Johanna T., who was herself a carrier. On March 30 two children of a widow living at Kolonowska were taken ill, and it is noteworthy that two workmen living in the same house were employed in the same mill as the meningococcus carrier, the father just referred to. Then followed two additional cases at Gross Stanisich, whose father had been working in close proximity to the house of Johann Ko. Later came still other cases which in turn could be connected with those mentioned above. As none of the relatives of the patient had been away from their houses or their places of work for weeks, the assumption would seem justifiable that the disease was introduced into the district by the woman X, who probably made a carrier of Albina's mother, and that from this focus still other carriers were produced through which the disease was ultimately conveyed to the various children mentioned.

Another interesting outbreak has been related by Rieger.¹² In this instance 19 cases developed between April 11 and May 11 among people who stand in some relation to a leather factory; 17 of these were children and 2 adults. Upon inves-

tigation it was ascertained that during the month of February already 4 cases had developed in the home of one of the workmen, St., of the leather factory, which was located in the village of Luisenthal, 5 km. distant from Brieg. Of these 4 cases 2 had died and 2 recovered, the true nature of the disease not having been recognized at the time. The husband had remained away from his work in the leather factory in order to help care for his family from February 24 to April 2, returning on April 3. On April 11, the first case of meningitis then developed at Brieg among the children of the workmates of St. It is possible, of course, that St. was a carrier and gave rise to other carriers in the factory, who in turn infected their respective families. On the other hand, a second possibility suggests itself. During St.'s absence three of his former workmates were taken ill with an inflammatory affection of the throat, accompanied by fever and the usual systemic symptoms, though without any signs of meningitis. The true nature of these cases was not ascertained, but on May 5 another workman was taken ill with the same symptoms and in his throat meningococci were demonstrated. It is thus possible that St. had nothing to do with the outbreak but that the disease was introduced by some other person with the production of carriers from that source. Regarding the possible manner in which the men were infected it is interesting to note that they all used the same drinking cup. The various patients were removed to a hospital, the common drinking cup replaced by fifteen separate cups and these disinfected after use, and the families of those who refused to go to a hospital were quarantined. The epidemic seemed to have come to a stop, as no further cases developed immediately after May 11. But on May 23 another child, whose father was employed in the same factory, was taken ill. It was then found that the suspected carrier St. daily brought sausage to the factory and sold this to his workmates. When this was stopped and the basket had been destroyed no additional cases appeared. This, of course, again suggests that St. was the original carrier and that the throat infection of the three men referred to above was not meningococcic in origin.

In fine it may be mentioned that none of the nineteen children had been in the factory, that some of them lived in Brieg itself and some in nearby villages, and that the infection must hence have taken place through the intervention of a healthy carrier.

Minor local outbreaks such as these are really very instructive, for they offer much better chances for discovering the manner in which they have been produced. In the first instance the chain of evidence seems quite satisfactory, and in the second sufficiently suggestive for all practical purposes, though one cannot help but wish that St.'s throat had been examined bacteriologically. Especially interesting in the second instance is the possibility that the drinking cup and the sausage may have served as vehicles in the dissemination of the organisms. The pernicious possibility of the first more particularly should ever suggest itself in the course of an investigation.

Further, interesting cases have been reported by Flack,¹⁷ as follows:

I. Sapper Bs. returned from France on April 9, 1916, and had been complaining of headache and pains in the back and legs while in the trenches a few days previously. There is no evidence that he had had any meningitis. Two days after his arrival one of his children was taken ill and removed to a general hospital with symptoms of cerebrospinal meningitis. Next day another child was taken ill and removed to an isolation hospital, where he died of the disease. The father was now isolated, and found to be a carrier of Type II meningococcus. A few days after removal, the first child was discharged after what was termed "an abortive attack" of cerebrospinal meningitis. He was brought by his sister on the Thursday. Up till then the sister had been quite well. She did not subsequently see her father at close quarters, but on the following Sunday she was taken ill in the morning and died within twenty-four hours. A swab from the child having the abortive attack showed the presence of the Type II meningococcus in the nasopharynx.

There had been no cerebrospinal fever in the borough for eighteen months until these cases occurred.

II. Private P., A.S.C., returned from France on leave on July 18. On July 27 one of his children was taken ill and died the next day of cerebrospinal fever. A swab from P. gave a plate showing many colonies of meningococcus (Type IV). His other three children were subsequently removed to a fever hospital. One child was suffering from pyrexia, with a temperature of 101° F., but no marked meningitic symptoms. The cerebrospinal fluid showed no cocci or increased cell content. From the fluid of a swollen knee-joint, however, the meningococcus was grown (Type IV). This appears to be an example of infection of the knee-joint without involvement of the meninges. A blood culture, taken one day after the knee had swollen, proved sterile.

III. Case 54 developed the disease at H. Military Hospital after he had been in there for two months on account of an accident. Of the four positive contacts, three were of the same type as the case. Two of these were in the beds on each side of the case, and the other was the staff nurse of the ward. All the available evidence went to show that the nurse was a chronic carrier, and inquiry revealed the fact that she had started nursing in the ward within two months, and had been nursing several cases of meningitis a year before and had not been swabbed subsequently. It seems probable that the case was infected by this staff nurse. The two other positive contacts cleared up quickly; the nurse is still a carrier.

The Recognition of Meningococcus Carriers.—The only way in which meningococcus carriers can be recognized is by a *cultural* analysis of the flora of the individuals' throats. A direct microscopical examination of the secretion is insufficient, as neither the form of the organisms, nor their location in reference to cells, nor their behavior to staining by Gram is sufficiently characteristic as to enable one to state with any degree of precision that one is dealing with the meningococcus or not. It is indeed rare that one does not find some organisms even normally which morphologically do not appear suspicious. No doubt the element of experience plays a great role in such examinations, but until this has been gained so many wrong diagnoses will have been made that the harm already done can scarcely be balanced by the good

accomplished later on. In the diagnosis of carriers of any kind, and particularly of such dangerous carriers as the types which we are now considering, the element of precision is all-important, and it is absolutely essential that no time be lost through uncertainty on the part of the observer. Particularly in times like the present, when an incorrect laboratory report may cause the most serious disorganization in our military camps and cantonments, only such methods should be employed as experience has shown to be reasonably reliable, even when used by observers of relatively little experience. To this end I can warmly recommend the cultural procedure suggested by Olitsky¹³ which is essentially based upon the partial elimination of those organisms which are most apt to cause confusion, by agglutination with normal horse serum, and the final identification of the meningococcus through its agglutination by a corresponding antiserum of high titer.

Olitsky's Method.—The initial steps of the method are those which have been in common use in the clinical laboratory before, viz., the preparation of plates of dextrose-serum agar, 0.4 per cent. acid to phenolphthalein, which are smeared with the secretion obtained from the nasopharynx of the suspected individual, incubated overnight and then subjected to a primary examination, to ascertain roughly how many different types of organisms are present, and particularly which ones resemble the meningococcus sufficiently as to necessitate a further analysis. Some of these initial steps require a more detailed consideration.

Preparation of the Medium.—So far as the preliminary medium is concerned, it should be remembered that ox blood cannot be used. The most convenient, because the most readily obtainable, is sheep serum. The sheep blood is collected at the slaughter house, allowed to clot and placed in the refrigerator until a sufficient quantity of serum has separated out. One volume of this is diluted with three volumes of distilled water and the mixture sterilized in an Arnold steam sterilizer by heating on three consecutive days for thirty minutes, or in the autoclave, at fifteen pounds' pressure, for forty minutes on a single occasion. This constitutes

Hiss's serum water, and is kept on hand in small flasks in appropriate amounts.

The *agar* is made from beef or bob veal infusion in the usual manner. It should be 0.4 per cent. acid to phenolphthalein and contain 1 per cent. of dextrose, which is added just before sterilization. The agar is tubed in 10 c.c. lots and the plates prepared when needed by melting the agar, cooling it to 50° C., when it is poured into the plates and 2 c.c. of serum water are added for every 10 c.c. of agar.

Slants of dextrose-serum-agar may be prepared in the same manner and can be kept on hand as such, provided that drying of the surface is carefully guarded against. The plates, however, are really what we need for our special purpose, and should invariably be freshly prepared.

Olitsky further recommends the use of 2 c.c. of a sterile 10 per cent. litmus solution in distilled water for every plate of 10 to 12 c.c. of the serum-agar, with the view of aiding in the differentiation between the meningococcus and the catarrhal micrococcus, the colonies of the former assuming a pink hue, while those of the latter are blue. Flexner¹⁴ states that this addition does not constitute as great an improvement over the colorless agar as might be supposed, as the freshly isolated meningococcus only possesses weak power of fermenting glucose, on the one hand, while certain streptococcus colonies assume a pink hue and thus confuse the plate. He adds, however, that on this medium the colonies of *Micrococcus flavus* present an opaque yellow or greenish appearance which is readily distinguished. Accordingly one can follow one's own inclination, the main point being to familiarize oneself thoroughly at the outset with the picture obtained from throats that are free from the meningococcus.

In the absence of sheep serum, horse serum to the extent of 2 per cent. may be substituted for the sheep serum water. Human ascitic fluid also furnishes excellent results, and Flexner warmly recommends defibrinated rabbit blood, of which 0.25 c.c., laked in 0.5 c.c. of sterile water, is placed in a plate, and there mixed with 10 c.c. of the melted glucose-agar, that has previously been cooled to 45° C.

The latter method may prove useful when isolated examinations are to be made, but when large bodies of people are to be examined the sheep serum medium is the most practical.

Inoculation of the Plates.—The plates, however they may have been prepared, are smeared with the secretion obtained from the individuals' nasopharynx. To obtain the latter it is most convenient to make use of the so-called *West tube*, which is pictured in the accompanying illustration:



FIG. 2.—West swab tube.

This is essentially a glass tube with thick walls, having an inside diameter of about 7 mm. and a length of about 16.5 cm., being bent near the one end to nearly a right angle. Through this tube passes a copper wire to which a smooth cotton swab has been fastened. The latter is pulled back into the tube sufficiently so that this can be plugged with cotton. A similar plug is placed in the proximal end. Thus prepared the tubes are sterilized by dry heat and can then be kept on hand in any desired number, until they are needed. Before use the guard plugs are removed, the bent end passed behind the velum palati, when the swab is pushed out, turned from side to side and again withdrawn into the tube. A plate being ready at hand, the swab is pushed out again, and the surface gently stroked, any particles of mucus that may be visible with the naked eye being further teased out on the medium with a platinum or nichrome wire. After inoculation the plates, properly labeled, are placed in the incubator, or if the examination has been made at a distance from the laboratory, in a metal box, which in turn is set in a vessel containing warm water, and transported as rapidly as possible. Under no circumstances should the swab be allowed to become dry before the inoculation, or the material or plate permitted to cool, for any length of time. Most failures at isolation of the meningococcus, when this is present, are due to oversight of these rules. It should further be remembered

that the meningococcus must be sought for in the nasopharynx, and that swabbing of the anterior and middle nares, as well as of the oral fauces only, serves no useful purpose. As the organism may, however, also occur in the crypts of the tonsils these should likewise be examined, a small swab being introduced into the anterior crypt more particularly, as deeply as possible, and a separate plate secured from this source.

Analysis of the Colonies Obtained on the Plates.—After incubating the plates at 37° C. for from sixteen to twenty hours (overnight), which may be followed by keeping them at room temperature for four to six hours further, during which time the colonies of the catarrhal micrococcus continue to increase in size and become opaque with sharply defined borders, the next step in the analysis of the plates constitutes Olitsky's method proper. This calls for 1 per cent. glucose broth—made from veal infusion—having an acidity of from 0.5 to 0.7 per cent. to phenolphthalein, to which 5 per cent. of unheated, sterile, clear normal horse serum is added. The mixture is conveniently placed in small tubes (8 to 10 mm. in diameter, with a length of 9 cm.) in 1 c.c. lots.

Suspicious-looking colonies are now fished from the plates and transferred to this medium—a colony to a tube—and incubated for twelve hours or overnight, if more convenient. During this incubation certain organisms, which may be mistaken for the meningococcus, grow in the medium in question, but being agglutinated at the same time leave the supernatant fluid clear or nearly clear. This group is termed the *normal horse serum negatives* and comprises the *Micrococcus flavus*, the *Micrococcus crassus*, the *Micrococcus pharyngis siccus* and an unclassified Gram-positive bacillus.* All such tubes, showing a clear supernatant fluid over the bacterial growth at the bottom, can be discarded at once. The remaining tubes in which the supernatant fluid is turbid may contain the meningococcus, the Gram-positive staphylococci, streptococci and the catarrhal micrococcus. After a little experience it will be possible to eliminate some of these also

* The influenza bacillus does not grow in this medium, because it contains no hemoglobin.

by direct inspection. The *Micrococcus catarrhalis* and the staphylococci grow with a dense turbidity and frequently show a pellicle on the surface. On shaking, the staphylococci, as well as the streptococci, will show an agglutinated sediment, while in the case of the meningococcus this emulsifies uniformly. The meningococcus tubes, moreover, show only a slight turbidity which, coupled with the appearance of the sediment on shaking, will mark these tubes as suspicious. To any such there is now added 0.1 c.c. of a 1 to 10 dilution in .85 per cent. saline of a polyvalent antimeningococcus serum of high titer. The tubes are next placed in a water-bath—not incubator—at 37° to 38° C. for two hours longer, during which time only those containing meningococci will clear up while the organisms are firmly clumped. The remaining tubes remain as before. From the tubes which have thus been found to contain meningococci smears for microscopic purposes, to demonstrate their Gram-negative nature, and subcultures for whatever additional purposes, may then be prepared, if desired, but not as a matter of necessity.

For rapid agglutination work, Krumwiede¹⁶ recommends the macroscopic slide agglutination test, which is conducted as described in the section on Typhoid Fever. He made use of curative horse sera with normal horse serum as control. Each serum should previously be tested against as many strains as possible to ascertain in what dilution satisfactory results can be obtained. In his experience a 1 to 50 dilution gave in general unsatisfactory results, while in 1 to 25 dilutions the clumps were lessened in size and some delay in reaction occurred—with some strains at any rate—but even so the results were, on the whole, fairly good. The best and most prompt agglutination, however, was gotten with dilutions of 1 to 10. Krumwiede (*l. c.*) further recommends the following as a subculture medium for testing out suspicious-looking colonies that have grown out on the initial plate: viz., a serum-water agar containing 1 per cent. of lactose, 1 per cent. of saccharose and 1 per cent. of Andrade's indicator, with the reaction set to this indicator. By the aid of this medium those mouth organisms can be excluded

which ferment one or both of these carbohydrates, and whose colonies accordingly will assume a pink or red tint, while the meningococcus colonies appear colorless.

As I have said before, Olitsky's method is very convenient for all purposes, and especially when a large number of individuals are to be examined in a short time. It leads to a definite result in fully a day less than any one of the procedures previously in use. But it calls for a certain amount of previous experience notwithstanding, to which end the beginner should familiarize himself with the behavior in pure culture, as well as in artificial mixtures, of the various types of organisms that may be met with in the throat and nose, before taking up the study of concrete cases.

The Management of the Meningococcus Carrier.—*Medicinal Treatment.*—Attempts to bring about the disappearance of the meningococci from the throat by local medicinal treatment have for the most part led to no satisfactory results. This corresponds to our experience with other types of carriers in which the upper respiratory tract is involved, and is, after all, what one would expect.

The best results have been obtained with chloramin-T, both by vaporization and by spraying. Gordon and Flack¹⁷ recommend an aqueous solution containing 2 per cent. of chloramin-T, a liter of which is steam-sprayed into a chamber of 750 cu. ft. capacity, in the course of from fifteen to twenty minutes, during which time the carrier remains in the room and inhales the disinfectant through the nose. One treatment is given a day. Of 14 individuals who were treated in this manner 11 are reported to have cleared up, the organisms in the majority of instances having disappeared by the ninth or tenth day.

Similar results were obtained with zinc sulphate, using a 1.2 per cent. aqueous solution. With heavily infected individuals, however, the number of necessary treatments was much greater.

A simpler procedure has been recommended by Dunham and Dakin¹⁸ as follows:

1. The nose is cleared with salt solution or with 0.25 per cent. aqueous chloramin-T solution either by spraying or

irrigation. The nose should be blown into a handkerchief between applications; and the chloramin-T solution should be used thoroughly as a gargle.

2. When the increased flow of secretion from the nose has subsided, the oil solution of dichloramin-T (see below) is applied with an oil atomizer. The oil spray should be repeated at intervals so as to make at least four treatments daily about equally spaced from each other. The spraying should be thorough and the oil carried to all parts of the membrane accessible. The first few applications of the oil sometimes occasion sneezing, but tolerance is soon acquired and subsequent applications cause no inconvenience.

3. The preparation of the dichloramin-T oil embraces three steps. First, the solvent eucalyptol (United States Pharmacopœia) is chlorinated: 500 c.c. are treated with 15 grams of potassium chlorate and 50 c.c. of concentrated hydrochloric acid for twelve hours or longer, and then well washed with water and with sodium carbonate solution. The water is drawn off and 15 grams of dry sodium carbonate are added to the oil and the whole is allowed to stand for twenty-four hours. The oil is filtered off, and dried with a little solid calcium chlorid, when it is ready for use.

Secondly, paraffin oil is chlorinated: To 500 c.c. of commercial paraffin oil, 15 grams of potassium chlorate and 50 c.c. of concentrated hydrochloric acid are added and the mixture is exposed to light, preferably sunlight, for several hours. It is then transferred to a separating funnel and washed successively with water, a solution of sodium carbonate, and again with water. The opalescent oil is drawn off, solid calcium chloride added, in small quantity, and about 5 grams of animal charcoal. On subsequently filtering through paper, a yellowish oil ready for use is obtained.

The third step is the preparation of the oil solution of dichloramin-T for use in the spray. Two-tenths gram of the dichloramin-T is dissolved in 2 c.c. of the chlorinated eucalyptol without heating. When the solution is complete, 8 c.c. of the chlorinated paraffin oil are added. After mixing, the solution is ready for use. The solution contains 2 per cent. of dichloramin-T. It is relatively unstable, and should

be discarded as soon as a distinct precipitate makes its appearance. An opalescence or moderate cloudiness is not evidence of material deterioration. It is a safe rule not to use the completed solution for more than three or four days after its preparation. It should be protected from strong light and is best kept in a cool place. Where large quantities are needed, a stock 10 per cent. solution of dichloramin-T in eucalyptol may be prepared and kept on hand in a cool, dark place for dilution with the paraffin oil, as 1 to 4, as required. The eucalyptol solution will suffer little deterioration in a month.

With the use of this spray it has been found possible to render the nasopharynx sterile in a few hours so far as the common aërobic bacteria of those structures are concerned. Only a small number of tests were made on meningococcus carriers, but so far as one can judge the results appear promising.

Quarantine.—Meanwhile the question practically resolves itself into two problems, viz., the possibility of preventing the development of passive carriers and the isolation of these when the condition has once arisen. The great difficulty in connection with the first problem is the fact that practically the entire entourage of a patient is apt to be already infected by the time that the diagnosis of meningitis is first made in the latter. That relatively simple precautionary measures would prevent the production of carriers is, however, well known, as is evidenced by the fact that in hospitals where such measures are employed the attendants upon meningitis cases rarely become carriers. It would accordingly be best to place all meningitis cases in a hospital and to quarantine the remaining members of the household until adequate bacteriological examinations have either proved that they are not carriers, or until the carrier condition is over. On paper this accordingly seems to be a very simple problem, and in connection with minor local outbreaks it *may* be a simple task. With major outbreaks, on the other hand, it is far from simple, and a problem which it may be admitted in advance has not yet been solved. Under any circumstances it should be remembered that a *local* investigation

for carriers does not answer the purpose. As I have said before, we may assume at once that the entourage is in the carrier stage already by the time that the nature of the malady is recognized in the patient. The question then is can we find out with whom these people have come into more intimate contact, since the carrier state has probably existed. If this number be small their examination and isolation would frequently still be possible and justifiable, but if it be large the problem is only too frequently beyond our control. Were we in the possession of a preventive treatment as in the case of smallpox, or even of typhoid fever, it is clear that the end would justify the enormous amount of work that would have to be done, and even so it might be argued that the investigation should be made and that the spread of the malady might yet be prevented, and in theory as well as in practice such might be the case. The management of every outbreak will have to be undertaken according to individual circumstances. The *sine qua non* of a successful campaign is, of course, the prompt reporting of all suspicious cases by the attending physicians. I have no doubt at all that much harm is here often done, partly through ignorance and partly through overconfidence on the part of the practitioner. But this applies to all of the infectious diseases, and is a problem *per se*. If once the disease has obtained a proper start in a community it must be remembered that there will be on an average ten carriers to a patient, and as carriers beget carriers it will become manifestly impossible to find them all, let alone to quarantine them all.

Public instruction and widespread bacteriological examination will have to be our mainstay, and will help us more to overcome a difficult situation than any other method. Public instruction should, however, not be confined to occasional lectures, but, in times of danger, to *daily* instruction, no matter how brief, regarding those methods of precaution which can be applied to everyone. This means, first and foremost, instruction regarding the manner in which the disease is spread and the necessary rules which follow. It means among other things that individuals must learn to restrain both sneezing and coughing; that irritative conditions call-

ing for either also call for medical treatment; that children are more susceptible than adults; that the common drinking cup and towel are an abomination; that coughing people should be excluded from the handling and preparing of food; that *a mask covering mouth and nose* can be had for a few cents and *probably represents the most effective single factor in preventing the spread of the disease* among those who are obliged to come in contact with it;¹⁹ and, *in fine*, that the individual who is wilfully or maliciously careless not only deserves confinement in quarantine, but should be so confined until he has learned wisdom or the danger is over.

Release from Quarantine.—When once quarantined carriers should not be released until at least three successive examinations, made at intervals of three days, have given a negative result.

I am fully aware that these suggestions seem to call for the millennium, but I am also fully aware that none better can be offered. The problem under existing circumstances cannot be solved in civil communities. Fortunately the predisposition to the disease is apparently much less marked than to the development of the carrier state, and even though a serious menace in our camps it is not likely to assume epidemic proportions there, which would be comparable to outbreaks in the civilian population, for the very reason that the most fertile soil for such an epidemic, viz., children, is here absent. In camps our mainstay must be an initial period of quarantine during which each individual is examined in reference to the carrier problem, just as he is examined physically; further, prompt bacteriological examination of every inflamed throat, whenever this may occur, isolation of all suspects and possibly prophylactic vaccination which may do much good and in any event can do no harm. As a *treatment* for carriers vaccination, of course, is perfectly senseless.

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BACILLARY DYSENTERY.

THE question whether or not bacillary dysentery *may* be disseminated through the agency of human carriers of the type that we are considering in the present volume, *i. e.*, of individuals who are themselves healthy and well, or at least not afflicted with the corresponding disease at the time, may be answered in the affirmative, though it must be admitted that it is probably very rare that the malady is spread in this manner.

Active Carriers.—It is now well known that bacilli of the dysentery group are particularly numerous in the intestinal contents during the initial period of the malady, when indeed they may be present in almost pure culture. That patients during this stage of the disease are very dangerous goes, of course, without saying. Subsequently, however, the number of the organisms rapidly diminishes, and during convalescence it is often very difficult to demonstrate their presence at all. That they *may* persist, however, for a variable length of time after the acute symptoms have disappeared has been shown by several investigators. Conradi¹ thus reports that in his experience the organisms continued to appear in the feces of practically every dysentery patient for at least a week or two after the clinical symptoms of the disease had subsided. He examined some 50 cases during the period of convalescence, and could demonstrate them in 27 as follows: in 11 mild cases from about the middle to the end of the second week of the disease, in 5 mild cases and 6 moderately severe cases during the third week; and in 1 mild case and 4 moderately severe cases at the beginning of the fourth week of the malady. In all these cases the stools still contained small particles of mucus, and it was in these that the organisms were found. Conradi mentions, however, that in some individuals he encountered them also

in feces that were apparently normal in every respect between the second and fourth week of the disease.

Pfuhl² reports having found the bacilli four weeks after the appearance of the initial symptoms in persons who had been suffering from a severe type of the disease and at a time when the stools were yet abnormal to a greater or lesser extent. Lentz³ found them in 3 out of 11 cases of so-called pseudodysentery* four or five weeks following "complete clinical recovery." An interesting instance has further been reported by Kruse,⁴ where bacilli were found in the stool eight months after an attack of pseudodysentery, during which time the individual had apparently been in perfect health. Kruse in commenting upon this case remarks that the person's health had in reality only been apparently normal, since the stools still contained mucus. How frequent such cases of long-continued elimination of dysentery bacilli are is not known. Kruse states that while no other instances had been recorded in the literature up to that time (1908) he believes that they cannot be so very rare, as his own case was met with in the course of a study of only about two dozen persons.

The *number of bacilli* which may be found in the feces of carriers of this type is probably always very small, and it usually requires a great deal of patience to demonstrate their presence at all. The elimination, moreover, may be intermittent, so that conclusions regarding their presence or absence should not be drawn from single examinations.

So far as the danger is concerned which such carriers represent, it is thought that this is but slight, for the reason that the number of organisms in the feces is so small. Kruse indeed thinks that as a menace to the health of others they are a negligible factor, so long as the carriers themselves do not develop relapses. But as this probability seems ever to be present, so long as the carrier state lasts, they after all

* The pseudo-group, so-called, comprises a group of organisms which differ from the Shiga-Kruse type in their agglutinative reactions, and unlike this type ferment mannite. This group comprises the *B. dysenteriae* Flexner, the Y bacillus of Hiss and Russell, Spronck's bacillus and others. Like the Kruse-Shiga type they are also pathogenic and produce the clinical picture of dysentery.

represent a potential danger of no small degree. It is thus interesting to note that at Poughkeepsie, where the disease had been epidemic during the summers of 1916 and 1917, new cases again appeared during the summer of 1918. It was then ascertained that in each case the patient was a member of a family in which the disease had occurred during the preceding summer, and that two persons at least who were ill with the disease at that time were carriers.*

Passive Carriers.—As regards the question whether *passive dysentery carriers* also exist, viz., persons who harbor the corresponding organisms in their intestinal contents, without having themselves passed through an attack of the malady, it would seem that such is also the case, although it must be admitted that this conclusion is based on a very small number of observations. Kruse⁴ himself, it is true, states that in the course of his own investigations which extended over a period of seven years, he was never able to demonstrate the presence either of true dysentery or so-called pseudodysentery bacilli in the feces of healthy individuals, or of persons who were suffering from maladies other than dysentery. Ford,⁵ on the other hand, claims to have found pseudodysentery bacilli in the intestinal contents of 10 out of 50 individuals who had died from various causes, but who had given no history of dysentery. But unfortunately he makes no statement regarding their serological reactions.

On the other hand, Duval,⁶ Jehle and Charleton,⁷ as well as Conradi,¹ have reported positive findings in a small number of children who had neither suffered from dysentery in the past nor were ill at the time of the examination. In Conradi's cases there was a definite history of contact with dysentery patients. Duval merely states that he could demonstrate the presence of pseudodysentery bacilli in small numbers in the stools of two healthy children, in whom the movements had been produced with the aid of a mild laxative. Unfortunately he does not mention how many individuals he examined. Jehle and Charleton likewise found pseudodysentery bacilli in two healthy children, while in

* Jour. Am. Med. Assn., 1918, vol. lxxi, p. 480.

many others negative findings were obtained. In all these cases the organisms were satisfactorily identified, so that there can be no question of the actual existence of carriers of this order. Nothing, however, is known regarding their number, and we can only say that while there is as yet no evidence that such carriers have initiated or extended an outbreak of the disease, this possibility exists at least in theory, and must be reckoned with in future studies of the epidemiology of the malady.

Manner of Infection.—As to the manner in which the disease could be disseminated by carriers we may imagine that this would probably occur as in the case of typhoid fever, viz., through contamination of foodstuffs and of drinking water. That infection may occur through a direct transference from the carrier to another person seems unlikely, in view of the small number of organisms that are usually eliminated. It would appear more probable that an outbreak of the malady itself would result if the organisms were first to find their way into a medium in which they could multiply, and which would then be used as food. Actual observations of this kind have, however, not yet been made, but the possibility is suggested not only on theoretical grounds, but also by the findings of Zinsser⁸ who could indirectly trace to the milk a small epidemic occurring in a hospital in New York City.

The Recognition of Dysentery Carriers.—*Technic.*—For the purpose of isolating the dysentery bacillus from the stools of carriers it is well to search for particles of mucus, and, if present, to transfer such to tubes containing approximately 5 c.c. of bouillon, in which adherent organisms are then emulsified by shaking. Otherwise one is obliged to start with the fecal matter itself, and to prepare an emulsion of this by rubbing up a bit, the size of a split pea, in about 10 c.c. of broth. In either case the search is then continued as described in the section on typhoid carriers, the Endo medium being well suited for plating purposes (which see). It is better, however, instead of making the reaction 0.2 per cent. acid to phenolphthalein, to have it just neutral, or at most very faintly alkaline. After incubating for twenty-four

hours the streaked plates are then examined. The dysentery colonies closely resemble those of the typhoid bacillus, and like these appear colorless, while the colon colonies are pinkish or red. Suspected colonies are now fished and subjected to a preliminary agglutination test, using a polyvalent antidysentery serum of high titer in a dilution of 1 to 100, as described (see p. 93). If a positive or a suggestive reaction is obtained, the organism is subjected to further study by cultural and serological methods, in order to determine the individual group to which the organism in question belongs. To this end the use of Hiss's carbohydrate serum water media* has been warmly recommended. The behavior of the different types is shown in the following table:

Group I	{ Shiga type Kruse New Haven	Ferment dextrose only with acid production, but without gas formation; lactose, mannite, maltose, saccharose and dextrin are not affected.
Group II	{ "Y" (His and Russell type) Seal Harbor Diamond Ferra	Ferment dextrose and mannite with acid production but without gas formation; lactose, saccharose and dextrin are not affected (maltose fermented after some days).
Group III	Strong type	Ferments dextrose, mannite and saccharose with acid production, but without gas formation; lactose, maltose and dextrin are not affected.
Group IV	{ Harris—Flexner type Gray Baltimore Wollstein	Ferment dextrose, mannite, maltose, saccharose and dextrin, with acid formation, but without gas production (saccharose usually fermented only after six days); lactose not affected.

More recent investigations have shown, however, that valuable as the carbohydrate method of classifying these various types has unquestionably been, it cannot be relied upon to the exclusion of serological methods. Thjötta⁸ thus has pointed out that the behavior both to maltose and saccharose may differ from one experiment to the other, that a different result may be obtained with solid and liquid media, with old and young strains of bacilli, etc.

The agglutinative behavior of the different groups toward

* The preparation of these media has been described on page 198.

their corresponding antisera is shown in the following table, the figures having reference to the degree of dilution in which positive reactions could be obtained.

	Anti-group I serum.	Anti-group II serum.	Anti-group III serum.
Group I . .	1 : 20,000	less than 1 : 100	less than 1 : 100
Group II . .	1 : 200	1 : 6400	1 : 400
Group III
Group IV . .	1 : 800	1 : 1600	1 : 3200

The agglutination test is carried out exactly as is usually done in the diagnosis of typhoid fever, the macroscopic slide agglutination method being used for purposes of orientation, and then followed either by the macroscopic test in various dilutions, in little tubes, or by the microscopic method, as one prefers, the former being the more convenient when large numbers of specimens are to be examined.

Management of Dysentery Carriers.—As regards the management of dysentery carriers practically the same regulations should apply as in the case of typhoid carriers, bearing in mind, however, that negative bacteriological findings in convalescents are of less significance than in connection with typhoid, for the reason that the organisms are much more apt to escape detection after the acute phase of the disease has been passed. For this reason it may be the safer plan to regard every dysentery convalescent as a potential carrier, irrespective of the bacteriological findings, so long as his stools are not free from mucus. Such individuals should be instructed regarding their possible danger to others; they should be excluded from participation in the handling of the food supply of communities as well as of families, and care should be had that their discharges do not contaminate the water supply. Actual quarantine will probably be necessary only very rarely.

In fine, it should be borne in mind that every dysentery patient is a potential focus for the infection of others, irrespective of the question whether these develop the disease themselves or merely become carriers. For this reason all those measures should be employed in safeguarding the patient's entourage which are used in connection with

typhoid, viz., screening, disinfection of stools, bed- and body-linen, the separate use of eating and drinking utensils, as well as their sterilization, and cleanliness on the part of the attendants. That notification of the health authorities should be practised and that these in turn should properly instruct the patient's family, goes, of course, without saying.

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ACUTE POLIOMYELITIS.

THE recognition of the fact that so-called acute anterior poliomyelitis is an infectious disease is of comparatively recent date and intimately connected with the discovery that the paralytic symptoms which in the past had been regarded as the essential feature of the disease in reality only represent an inconstant phase: that, in fact, there are many cases in which paralysis never occurs. The first observer to call attention to this possibility was Caverley,¹ who in his report on the Rutland epidemic of 1894 states specifically that 6 cases had no paralysis, but showed the same group of symptoms as were noted during the initial stage of those who subsequently did become paralyzed, viz., "headache, fever, convulsions or nausea, one or all."

The significance of these abortive cases, however, was not recognized until Wickman,² in 1905, emphasized their occurrence and established their role in the dissemination of the disease beyond any reasonable doubt in so far as this was possible at a time when the causative agent of the malady and the possibility of its transmission to laboratory animals had not yet been discovered. These links in the evidence which were necessary to ultimately prove the infectious nature of the disease have since been supplied. In 1908 the malady was thus experimentally produced in monkeys by Landsteiner and Popper,³ and shortly after by Knoepfelmacher⁴ abroad, and by Flexner and Lewis⁵ and by Strauss and Huntoon⁶ in the United States. Its transference from one animal to another was achieved almost immediately thereafter by Flexner and Lewis⁷ in New York, Leiner and Wiesner⁸ in Vienna, and Landsteiner and Levaditi⁹ in Paris. As regards the nature of the organism in question, Landsteiner and Levaditi,¹⁰ as well as Flexner and Lewis,¹¹ then showed that it is not a bacterium but belongs to the group of the so-called filterable viruses. Its cultivation was

achieved by Flexner and Noguchi¹² in 1913, and typical lesions and death produced in monkeys with cultures that had been carried as far as the eighteenth generation.

Laboratory investigation had thus fully substantiated the correctness of Wickman's assertion that acute anterior poliomyelitis is indeed an infectious disease, and the foundation had been laid for the further investigation of its epidemiology by laboratory methods. This, however, has been attended with peculiar difficulties, for in so much as we are not yet in possession of any other method for the identification of the virus in question than the animal experiment, progress has of necessity been slow. But even so enough has been learned to warrant the conclusion that in the dissemination of this disease also human carriers play a dominant and possibly the only role. This view has been combated by a number of observers, and the hypothesis advanced that insects and notably the common house and stable fly act as distributors of the virus,¹³ but it was shown that while these may indeed mechanically carry the organism,¹⁴ its actual transmission in this manner to either a human being or a susceptible animal has not yet been demonstrated. On the other hand, Flexner and Lewis¹⁵ have shown that not only the probable portal of entry but that of exit of the organism, is the upper respiratory tract, for they were able both to successfully infect monkeys through the nasopharyngeal mucosa and to recover the virus from the nasal mucosa, even though the inoculation had been made through other channels. Conditions here are thus very similar to those which have been shown to exist in meningococcus meningitis, where Flexner¹⁶ could demonstrate that following intraspinal inoculation the corresponding organisms subsequently appeared both free and enclosed in leukocytes in the nasopharynx.

Corresponding studies in the human being revealed analogous conditions. It was thus found that here also the virus may be demonstrated by inoculation tests, both in the mucous membranes of the nasopharynx and in the nasopharyngeal secretion,^{17 18} as well as in the tonsils^{19 20} of patients who had died during the acute period of the malady.

Active Carriers.—Subsequent investigation then showed that the virus may persist in the nasopharyngeal secretion of recovered cases for a long time while retaining its virulence not only for monkeys but also for human beings. Kling, Pettersen and Wernstedt²¹ have thus reported an instance in which the virus could be demonstrated in the nasopharyngeal swabbings and washings as late as 204 days (seven months) after the infection, and Lucas and Osgood²² have described a case in which they found the virus in the nasal secretion of a child, four months after an attack. The same child had had an attack of the disease two years before, and the writers are inclined to think that it had harbored the organism during this entire time, and that the second attack was an exacerbation of the first. The same investigators had previously established that in recovered monkeys also the virus may be present for five months following an acute attack of the disease.²³

That recovered convalescents who have actually been paralyzed may thus become carriers can hence be regarded as an established fact. But striking though this demonstration has been, even more important is the discovery that the carrier state may also develop in the so-called, though wrongly termed, abortive cases, in which no paralytic symptoms develop. For these cases are after all far more dangerous to the community than the former, as they are very likely to be overlooked and to be wrongly interpreted not only by the parents but also by the attending physician, and especially so at a time when the disease is not occurring in epidemic form or when an epidemic has just begun. We now know that in the course of an epidemic these non-paralytic cases represent a very large proportion of the total number of infections. During the great Swedish epidemic Wickman² thus came to the conclusion that from 25 to 56 per cent. of the total incidence of the disease was of this order, and expressed the belief that these figures even were probably too low. Müller,²⁴ while investigating an epidemic occurring in Hessen-Nassau, came to a similar conclusion. The commission appointed by Surgeon-General Blue, of the United States Public Health Service, to investigate the big

New York epidemic of 1916, reported that the disease was "widely prevalent and most frequently of the non-paralytic type."²⁵

That abortive convalescents may also harbor the causative organism in their nasopharyngeal secretions has been shown by Taylor and Amoss.²⁶

Passive Carriers.—In addition to convalescent carriers the existence of passive, healthy carriers of the poliomyelitic virus has also been demonstrated. This was first accomplished by Flexner, Clark and Fraser²⁷ and subsequently confirmed by Kling and Pettersen²⁸ abroad and by Taylor and Amoss²⁶ in the United States.

In view of the cumbersome and expensive method which is unfortunately the only one thus far available for the purpose of demonstrating the presence or absence of the virus, viz., the inoculation of monkeys, a sufficiently extensive series of investigations to determine the average duration of the carrier stage, the incidence of abortive and paralytic, as well as of healthy carriers, has thus far not been possible. But the evidence which is actually available is sufficient to show the very real menace which the carriers represent not only in a community, but even to themselves, as is shown by the following examples:

A little girl, aged four years, was taken ill on October 12 and admitted to the Rockefeller Hospital on October 17, where she was found to be suffering from severe anterior poliomyelitis. She was discharged on October 28. The child's parents were subjected to a nasopharyngeal irrigation with normal saline, 150 c.c. of washings being obtained. This material was shaken and passed through a Berkefeld filter. 1.5 c.c. of the filtrate was injected into the sheath of each sciatic nerve and 140 c.c. into the peritoneal cavity of a *Macacus cynomolgus* (monkey A). On November 11 the animal was noted to drop his right leg. On November 12 this was flaccid and lumbar puncture yielded 2.5 c.c. of fluid containing an excess of leukocytes. On October 13 the animal was killed. Examination of the cord, medulla and interstitial ganglia showed lesions typical of acute poliomyelitis. On December 3 two monkeys (B and C) were injected intraneurally and intra-

peritoneally with a glycerinated emulsion of the spinal cord and medulla of animal A. On December 10 examination of the spinal fluid of C showed an excess of leukocytes, and on December 13 both legs were partially paralyzed. The animal was killed on December 13. In monkey B paralysis of the legs appeared on December 19; on December 21 the arms and back were weak and the paralysis was extending. The animal was killed on December 23. Examination of the cord and medulla and ganglia showed the typical infiltrative degenerative lesions of poliomyelitis.

Still other animals were subsequently injected with glycerinated emulsions of the nervous organs from B and C, and typical results obtained in these also. (Flexner, Clark and Fraser.)

The investigation thus conclusively showed that one or both of the little girl's parents harbored the virus of the disease in the nasopharynx, and evidently was a healthy carrier, as neither showed any symptoms of illness at the time of the examination.²⁷

A similar instance of the presence of one or more healthy carriers in a family where active poliomyelitis had occurred has been described by Kling and Pettersen.²⁸

The patient in this case was an adult, aged forty-one years. He was taken ill on September 10; both legs became paralyzed on September 12 and death occurred on September 14 from respiratory failure. The man's family consisted of a wife and three children, all of whom remained well. Nasal washings in distilled water were obtained from all of these on the day following the death of the father. Combined, they amounted to one liter. This material was concentrated in the vacuum at 35° to 38° C. to 75 c.c., treated with the requisite amount of sodium chloride and filtered through a Berkefeld filter. A monkey (*Macacus sinicus*) was injected on September 20 intracerebrally with 0.5 c.c. and intraperitoneally with 20 c.c. of the filtrate. Death resulted on October 2, both legs and the back being paralyzed. Sections of the cord showed moderate perivascular and diffuse infiltration of the nervous tissue with mononuclear cells and neurophagocytosis. On October 3 a second *Macacus* was

inoculated with an emulsion of the spinal cord of the first animal. Paralysis of the right leg occurred on October 13 and of the left on October 14. The animal was killed on October 15, sections revealing typical lesions of poliomyelitis.

*Example, Illustrating the Possible Development of Poliomyelitis in a Carrier, Who was not Ill at the Time of the Examination*²⁶ (Taylor and Amoss).—On June 2, 1917, a youth, aged sixteen years, living at Waitsfield, Vt., attended a ball game at Northfield, Vt., and on his return home stopped in Montpelier for supper. At the time poliomyelitis existed at the latter place, but there had been no cases either at Waitsfield or at Northfield. On June 12 he was taken ill with headache, pain in the back and legs and vomiting; on June 13 he was found to have fever; by June 16 there was extensive paralysis involving both legs, the right triceps, the intercostals, pectorals and diaphragm. Examination of the spinal fluid showed the presence of 400 leukocytes per c.mm. and an excess of globulins. Death occurred on this date.

The youth's family consisted of his parents, a sister (Hazel), aged thirteen years, and two brothers, aged ten and seven years, respectively. The two younger brothers (Everett and Dwight) slept in the same bed and in the same room with the elder brother. On the day of the latter's death Everett and Hazel were separately given a nasopharyngeal irrigation with distilled water; 60 c.c. were obtained from the one and 100 c.c. from the other. The material was treated with 10 per cent. of ether (which inhibits bacterial development, but leaves the poliomyelitis virus uninfluenced), shaken for two and a half hours with glass beads, centrifugalized, filtered through a Berkefeld filter and concentrated in the vacuum at 35° C. to about 2 c.c. One monkey (A) was injected with the concentrate obtained from the one child (E) and a second monkey (B) with that corresponding to the other (H). Neither child had been away from Waitsfield, and Hazel had been perfectly well at the time the washing was taken. Everett, however, was taken ill on the same day as his elder brother. He had fever and diarrhea, but recovered quickly, and on subsequent examination

showed no signs of paralysis or muscular weakness, and no abnormality of the reflexes.

Hazel was taken ill with fever and headache on June 21; on June 22 the reflexes were increased: there was stiffness of the back but no muscular weakness. These symptoms subsided gradually, but on reëxamination on July 22, partial paralysis of the left deltoid, the right anterior tibial and of the abdominal muscles could be detected, so that there can be no doubt that she had passed through a mild attack of the disease.

The two monkeys developed typical paralysis. A was not killed, but later, when the paralysis had become stationary, it was injected intracerebrally with a large dose of an active virus, with a negative result, showing that it had developed a high degree of immunity. B was killed and a third monkey C was inoculated with an emulsion of B's spinal cord and medulla, which resulted in paralysis and typical focal lesions.

The third child (Dwight) was taken ill on June 18 with the same disease, and recovered following treatment with the serum from a recovered case. An examination of the nasal washings about two and a half months later gave a negative result.

These findings suggest, of course, that the elder brother was infected either at the ball game or at Montpelier. Before falling ill himself he evidently conveyed the virus to one or more members of his family, with the result that all the children became infected. Everett's case may possibly be viewed as an abortive case of the disease, while Hazel at the time of the examination evidently was a healthy carrier who subsequently developed the disease herself.

In connection with the recital of these findings, Taylor and Amoss have raised the question whether in the final analysis every case of poliomyelitis may not develop from a carrier; in other words, whether a "carrying period" does not precede the outbreak of the malady in every case. As a matter of fact, such a view is not a startling one, and the observation in itself is quite in accordance with what has been noted in connection with typhoid fever, diphtheria, pneumonia, camp septicemia and meningitis.

Ogilvy³³ states that the epidemic which occurred at New Rochelle in 1916 and which gave rise to 125 cases of the disease was definitely traced to a carrier coming from an infected household in Brooklyn.

Frequency of the Carrier State; Relative Insusceptibility to the Disease.—As regards the frequency of occurrence of poliomyelitis carriers, I have already pointed out that we have not as yet the necessary laboratory data to make any definite statement. But bearing in mind, on the one hand, the large number of non-paralytic cases which have been noted in the course of an epidemic, and, on the other, the relatively slight susceptibility to the disease on the part of those who are exposed, which Herrman²⁹ has estimated at not more than 2 per cent., as contrasted with measles (90 per cent.), whooping-cough (75 per cent.), scarlet fever (25 per cent.) and diphtheria (20 per cent.), it would seem reasonable to suppose that *the number of carriers and above all of passive carriers must be far greater than the number of actual cases*. Evidently the transmission of the organism from one person to another must take place very readily. We have thus seen that the elder boy of the family, studied by Taylor and Amoss, was able to infect his two younger brothers and sister either directly or indirectly within two weeks after his own and evidently very brief period of exposure on the day of the ball game. As a matter of fact, Everett and Hazel were carriers at that time, and may have been such even at an earlier date. The interesting question, of course, immediately arises: Why is it that the incidence of morbidity is so small in view of the ready transmissibility of the virus? This question, in a more or less modified form, of course, comes up for consideration in connection with the carrier problem in its relation to other infectious diseases. But whereas we know nothing whatever of the causes of this relationship in the other diseases which we have been considering, we have some information at any rate bearing on this problem in poliomyelitis, as will appear from the following considerations:

The Inactivating Power of the Nasal Secretion upon the Virus of Poliomyelitis.—As the virus of poliomyelitis is found in the

nasal secretion of infected individuals, and as the disease may be produced through nasal inoculation, the thought has naturally suggested itself that if the disease does not develop in spite of the presence of the organisms in the nasopharynx, as in the case of healthy carriers, this might possibly be due to some property inherent in the nasal secretion itself. Such a hypothesis, of course, has many attractions, as quantitative differences in the degree of the inactivating or neutralizing power of the secretion would readily explain the development or non-development of the disease, the duration of the period of incubation and other factors, concerning which we have hitherto been completely in the dark.

The problem in question has been studied by Amoss and Taylor.³⁰ These investigators have found that the washings from the nasal and pharyngeal mucosa of certain individuals actually possess the power to inhibit the infectious action of active poliomyelitis virus. To a certain extent this property seems to depend upon the integrity of the nasal mucosa, for of 8 normal adults, 6 furnished a material which protected the animal completely against a double lethal dose of the virus, while that obtained from the remaining 2 furnished no protection. Rhinoscopic examination showed that the anatomical condition of the nasopharynx in the latter 2 was definitely abnormal. Amoss and Taylor conclude that while a distinct abnormality, such as an acute pharyngitis or rhinitis, may lead to a disappearance of the inactivating power, and with a return to the normal of the nose and throat, there must be still other factors involved of which we know nothing as yet, as fluctuations were also observed irrespective of the existence of any colds and the like. The fact remains, however, that the secretions in question frequently do possess the power to inactivate poliomyelitic virus, and it remains to be seen just what the findings will be in a series of healthy carriers, convalescent carriers, as well as during the different stages of the acute malady. It will be necessary, moreover, to ascertain whether in children, who are notoriously susceptible to the disease, the inactivating property is more apt to be wanting than in adults. In the one child which was studied by Amoss and Taylor during

the acute period of the disease the washings did not neutralize the virus. In another child, in which the examination was made on the fifteenth day of the attack, neutralization occurred. Neither one of the two had received immune serum. In a third child which had been treated with serum, protection was noted during the acute attack. The mixed washings from the children Everett and Hazel, referred to above, failed to neutralize the virus. This examination was made a month following Hazel's attack, and hence at a time when immunity must have existed. For this reason it is scarcely admissible to ascribe the neutralizing effect in the second case, just referred to, to that factor. It would be interesting to know whether the virus was still present in these various cases at the time of the examination. As the nasal washings were fractionally sterilized by heating at 60° C., the neutralizing effect upon the added virus cannot, of course, be taken to indicate that the child in question was not a carrier.

Manner of Infection.—As regards the manner in which infection is brought about, be this through an active case or a carrier, nothing definite is known. All that we can say is that poliomyelitis evidently belongs to that group of diseases in which infection takes place through the upper respiratory tract, and that the mode of infection is hence very likely the same as in meningitis, diphtheria, pneumonia and camp-septicemia. We may accordingly assume that the virus is transferred either directly through sputum spray, in whatever manner produced, or indirectly through the common use of eating and drinking utensils, through toys and the like, and possibly also through the inhalation of virus-laden dust. This latter possibility is suggested by the experiments of Neustaedter and Thro.³¹ That the fly also *may* play a role in the transference of the virus has already been pointed out, although no instance has as yet been observed in which this has actually been proved.

Maintenance of the Carrier State.—While we can readily see how the virus of poliomyelitis may be transferred from one person to another, we are as yet in complete ignorance regarding the conditions which make it possible for the organism to maintain itself in the nasopharynx. We have seen

that normally the nasopharyngeal secretion is very apt to exercise a neutralizing effect upon the virus, in so far at least as its power to produce disease is concerned, but it is not known whether this inhibitory action is also directed against the growth of the organism *in situ*. Conceivably its penetrating power might be affected, without impairment of its vegetative activity. However this may be, we are practically driven to the assumption that the poliomyelitis organism also finds its habitat in those structures of the upper respiratory tract which we have come to regard as the home of the meningococcus and the diphtheria bacillus in the corresponding carriers, viz., the lymphatic tissue. As a matter of fact, it has been shown by various observers^{19 20} that the tonsils of fatal cases contain the virus of poliomyelitis, and Lucas and Osgood³² have succeeded in demonstrating its presence in the tonsils of recovered monkeys.

Demonstration of the Carrier State.—Unfortunately the only method which is thus far available to demonstrate whether an individual is or is not a carrier of the poliomyelitic virus is the animal experiment. The details of this procedure have already been given and need not be repeated at this place (see above). It is, of course, self-evident that such a cumbersome method, however important it may be for the purpose of investigating the various phases of the epidemiology of poliomyelitis, is almost useless when it comes to the practical control of an outbreak of the disease on a large scale.

Management of the Carrier.—While we are not in the possession of a practical laboratory method by which we may determine whether or not a person is a carrier, or when the carrier stage has ended, we now know enough of the nature of the disease and its method of dissemination as to enable us to formulate certain general rules of control which will suffice to keep the malady within bounds if properly enforced.

Quarantine.—As the patient himself is the primary focus of dissemination, hospitalization should be enforced whenever home conditions are such as to render the individual isolation from the remainder of the family impossible. In this manner the number of healthy carriers whom we must regard after all as the greater menace will of necessity be diminished,

care being taken, of course, that at the hospital also suitable precautions are maintained to guard against the development of carriers among the attendant personnel (gowning, capping, masking). When hospitalization cannot be carried out, isolation of the patient and his nurse should be insisted upon, with a release from quarantine of those who do not come in contact with the one or the other, while rigid quarantine of the entire household should be enforced if isolation of the patient is not possible. Quarantine, when it is deemed necessary, should be extended particularly to children, either of an infected house, or an infected neighborhood, or of an entire community, according to the urgency of the situation.

Regarding the *duration of quarantine* three weeks is now regarded as sufficient. This view is, of course, not based upon the results of laboratory work but upon general epidemiological observations. Shaw²⁵ reports that an analysis of 36 primary and secondary cases showed that the longest period that a primary case was actually observed to be infectious was eight days, and in most cases only one or two days, so that three weeks would render ample and sufficient protection. That this *may* suffice for most cases is undoubtedly true, but that the chronic carrier will escape under this regulation is also unquestionable. But unfortunately we have no alternative so long as we have no practical method available for determining whether a person is still a carrier or not.

It has been suggested that in the management of an epidemic passive immunization of exposed individuals with the serum of recovered cases would appear to be indicated. This seems logical and should be carried out whenever possible, bearing in mind, however, that passive immunization can hardly be expected to affect the carrier state and that quarantine and disinfection must be our mainstays of defense.

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PNEUMOCOCCUS PNEUMONIA.

IN view of the rarity with which pneumonia was known to develop through contact, and the presence, in the mouths of a large percentage of healthy individuals, of pneumococci which supposedly did not differ from those found in pneumonic lungs, it was generally and not unnaturally assumed in the past that the outbreak of the disease in an individual took place in consequence of an auto-infection. The situation, as formerly understood, might well be compared to the presence about the body of many persons of some high explosive, the detonation of which might lead to the individual's destruction at any time. According to this view all persons harboring the pneumococcus in their mouths truly lived constantly with the sword of Damocles suspended above them.

Varieties of the Pneumococcus in Their Relation to Pneumonia.—This idea had to be abandoned, however, when it could be shown that although culturally and morphologically pneumococci might appear alike, differences exist, nevertheless, which are sufficiently marked and constant as to warrant a division of these organisms into different groups. In the United States, Dochez and Gillespie¹ thus showed that the pneumococci derived from cases of lobar pneumonia may be roughly divided into two groups, of which the larger, comprising about 80 per cent. of the strains, can be further divided into three smaller groups, which were termed groups I, II and III, respectively. The remaining 20 per cent. correspond to group IV. In their earlier work Dochez and Gillespie demonstrated that groups I and II gave perfectly distinct immunological reactions, while group III was separated from these, as well as from group IV, on morphological and cultural grounds. Hanes² subsequently showed that representatives of the third group also can be distinguished from the remainder by specific serum reactions. These three

types are now viewed as constants and can readily be distinguished from each other, and the fourth group, which latter seems to consist of a series of independent varieties that do not cross in their immune reactions either with representatives of groups I, II and III or with each other. Still later Avery³ found that among the representatives of group II there are certain ones which, while conforming in a general way to the second type, yet differ from this and from each other. These he termed II a, II b, and II x.

Similar studies made in Germany by Neufeld⁴ showed that pneumonia there also was in part associated with pneumococci of the American types I and II, and much earlier Schottmüller⁵ had already drawn attention to the fact that the pneumococcus mucosus (American type III) may be the causative agent of lobar pneumonia. In South Africa, Lister⁶ encountered five groups of pneumococci in pneumonia patients, of which three are identical with types I, II and III of the United States and of Germany, while the other two have not yet been found outside of South Africa, and of these one group appears to be dominant among the lobar pneumonias of that country.

On studying the distribution of the four American types, Dochez and his collaborators Gillespie and Avery⁷ found that in New York 145 cases of the disease could be classified as follows:

	1912-13, per cent.	1913-14, per cent.	Average, per cent.
Group I	47	30	38.5
Group II	18	39	28.5
Group III (mucosus)	13	8	10.5
Group IV (heterogeneous)	22	23	22.5

Corresponding figures have since been obtained by Clough,²⁶ Sydenstricker and Sutton,²⁵ Hartmann and Levy,²⁷ and others.

On extending their studies to the flora of the mouths of healthy individuals and taking care to exclude, as far as possible, persons who had been in direct contact with pneumonia, Dochez and Avery⁷ then found that the pneumococci which were here encountered almost invariably were of the heterogeneous order, which seem to be responsible for roughly

20 per cent. of the cases of lobar pneumonia, while organisms belonging to the fixed types were only exceptionally met with. They showed, furthermore, that as convalescence proceeds in those cases in which fixed types were found while the disease was in actual progress, these disappear and are replaced by organisms which are indistinguishable from those found in the mouths of normal persons.

As detailed studies, moreover, furnished no evidence that a mutation of pneumococci takes place in the course of an infection, the writers very properly conclude that our former concept regarding the origin of pneumonia is no longer tenable for at least 75 per cent. of the cases.

Active Carriers.—In view of the rapidly accumulating evidence connecting the dissemination of various infectious diseases with healthy human carriers, the idea naturally suggested itself that in the fixed types of pneumonia, at any rate, carriers might also play a role. That *the convalescent pneumonic may indeed be a potential carrier* was found by Dochez and Avery⁸ quite early in the course of their investigations. For in studying the disappearance of the fixed types and their replacement by organisms belonging to group IV they observed that while the fixed types *may* disappear as early as the twelfth day after the onset of the malady, they may remain much longer, and in 4 instances, *i. e.*, in 20 per cent. of their first series of 20 cases, type organisms were still present at the time that the patient was lost to observation—a period varying between thirty and ninety days from the onset of the disease.

Passive Carriers.—The epidemiological significance of these findings was then further emphasized when the same observers could show that whereas organisms belonging to groups I and II are found only very exceptionally in the mouths of individuals who have not been in contact with pneumonia, they are quite commonly met with in persons who have been in close contact with patients suffering from the disease in question, and that the type corresponds to that of the patient. They thus found that among 41 contacts corresponding to 30 patients who harbored either type I or type II, the corresponding type was present in 13. This means that

for every 100 patients of this order we may assume the existence of 43 carriers harboring the same type of organism. As the latter were found to remain in the throats of such individuals for a period of time varying between seven and forty-five days, and as the types in question are responsible for some 60 per cent. of the pneumonia cases and the majority of the deaths resulting, the conclusion suggests itself that *the dissemination of pneumonia of this order may occur in a manner analogous to the dissemination of meningitis, diphtheria, typhoid fever, cholera, etc.; in other words, through carriers, which here as there may be convalescents from the disease, but which for the most part probably are apparently normal individuals, who have acquired the carrying state through contact.*

Later investigations have largely confirmed these earlier findings. Stillman^{9 10} in his analysis of 454 cases of *lobar pneumonia* admitted to the wards of the Hospital of the Rockefeller Institute during a period of five years thus found practically the same distribution of types as that originally given by Dochez and his co-workers (see above). The following table represents an analysis of 19 cases in which the sub-types IIa, IIb and IIx are also considered:

	No of cases.	Percentage.
Type I	151	33.26
" II	133	29.29
" II a	6	1.32
" II b	4	0.88
" II x	9	1.98
" III	59	12.99
" IV	92	20.26

A further study of the varieties of pneumococci found in *normal mouths* was based upon 297 individuals who had not been in direct contact with lobar pneumonia. Of these 116, *i. e.*, 39 per cent., harbored organisms of the pneumococcus type, and they in turn could be classified as follows:

	No. of cases.	Percentage.
Type I	1	0.8
" II	0	0.0
" II a	1	0.8
" II b	7	5.8
" II x	14	11.6
" III	34	28.1
" IV	64	52.9

These findings are in striking contrast to those which were obtained in an analysis of 184 normal individuals *who were known to have been in contact with lobar pneumonia* of types I or II.

	Total No.	No. infected.	Per cent.
In contact with type I	107	16	15
“ “ “ “ II	77	5	6
<hr/>			
In contact with types I or II	184	21	11

It will be noted that whereas among non-contacts only 0.8 per cent. of the cases examined harbored organisms of types I and II, among known contacts this figure rose to 11 per cent.

Frequency of Passive Carriers.—A very good idea of the extent to which pneumococci of the fixed types probably occur among the inhabitants of a large community is afforded by Stillman's analysis of the saliva of 942 normal individuals, selected at random, but including the series of contacts just considered. Pneumococci were found in 450 instances, *i. e.*, in 47 per cent. Type analysis gave the following results:

	No. of cases.	Percentage.
Type I	34	7.0
“ II	22	4.5
“ II a	1	0.2
“ II b	26	5.3
“ II x	47	9.7
“ III	85	17.5
“ IV	271	55.8

In commenting upon these findings, Stillman states that of the 34 cases in which type I was found 33 had been in intimate contact with lobar pneumonia of the same type. Of the 22 individuals harboring type II 19 had recently been in close contact with pneumonia of that type.

Regarding the significance of the occurrence of types II b, II x and III in normal individuals, Stillman concludes that they must be viewed as normal inhabitants of healthy mouths and that their import is essentially the same as that of type IV, bearing in mind, however, that type III, when it does cause pneumonia, produces a form which is more fatal than any other, giving a mortality of some 60 odd per cent.

An interesting analysis of the types of pneumococci which may be found in individuals who at the time are not suffering from pneumonia has further been made by Miriam Olmstead.¹¹ Her series comprises 2477 surgical cases of all kinds who were examined for types before operation, with the idea of ascertaining the relationship of postoperative pneumonias to the organisms that were present before surgical treatment was instituted. Of this number 798, *i. e.*, 32.2 per cent., harbored pneumococci at the time of examination, a type analysis of which gave the following results:

	No. of cases.	Percentage.
Type I	5	0.6
" II	10	1.2
Atypical II	90	11.2
Type III	104	13.0
" IV	589	73.8

Of the 5 individuals harboring type I, one gave a history of contact with a case of pneumonia, and this was the only one of that order that developed postoperative pneumonia.

From these data we may conclude that, as Dochez and Avery first claimed, types I and II are indeed practically only found in patients and convalescents of those types, and in individuals who have been thrown into more or less intimate contact with such cases, and it would follow that we may rightfully regard individuals harboring these organisms, be they convalescents or healthy, as carriers, comparable to other human carriers of infectious disease, and hence as important factors in the dissemination of lobar pneumonia of these types. This being so, we may assume, as in the case of other infectious diseases of this order, that the danger arising from the patient himself is in all probability less than from the healthy carrier, as the former is confined to his bed and is brought into contact with relatively few persons only during the greater period of his carrying stage, while the healthy carrier mingles with the community at large. The latter is not conscious of his fatal gift; moreover, he is not suspected by others, and is no doubt capable of producing still other carriers, so that through him individually or through such secondary carriers a widespread dissemination of the organisms may occur, and thus reach susceptible indi-

viduals in whom the disease itself then develops. That the carrier himself does not necessarily fall ill of pneumonia has been definitely established, but that he may do so is shown in the protocols accompanying the papers of Dochez and his co-workers.

Duration of the Carrier State.—As regards the duration of the *carrying* period for types I and II on the part of normal individuals, Stillman found as average for the former twenty-five days and for the latter forty-three days. The longest period was eighty days (in a type I case).

Common Colds as Sources of Pneumonia.—In this connection it is interesting to note that pneumococci of the fixed types *may* be encountered in the nasal secretion and sputum of ordinary colds, in the absence of any history of contact with pneumonia cases. Such individuals may accordingly be regarded as potential sources of infection for others. In a study of 65 cases of common colds Valentine²⁸ thus found pneumococci in 37 by animal inoculation, and in 6 additional cases by plating on blood agar. Of the total of 43 cases, 2 were of type I, 2 of type II, 4 of type III and 35 of type IV. The 2 cases of type II and 1 of type III gave a history of contact with pneumonia, while in the remaining cases of the fixed types no such history could be obtained. In 1 of the type I cases the corresponding organism could be demonstrated even after a year.

The question, of course, arises whether these cases were not all contact, *i. e.*, passive carriers, even though no history of contact could be obtained. On the other hand, the idea suggests itself that cases of this order may be comparable to cases of meningococcus pharyngitis, *viz.*, that in addition to the orthodox picture of a pneumococcus infection of the lung, there may be milder types in which only the upper respiratory tract is involved, and that in addition to the carriers convalescent from the severer malady, there may be carriers resulting from the minor infections. The fact that the organisms were found by Valentine in large numbers suggests that the latter possibility indeed exists.

Habitat of the Organisms.—Regarding the habitat of the pneumococci in healthy carriers our knowledge is practically *nil*. The results reached by the investigators mentioned in

the foregoing pages have reference either to cultures taken from the saliva or the sputum, but this does not of necessity imply that the organisms multiply on the free mucous surfaces. From corresponding observations made in connection with diphtheria and meningitis we have reason to assume that organisms found upon the free surfaces are there more or less accidentally, and that their actual habitat is in the crypts of the tonsils or the various nooks and corners connected with other lymphatic structures of the throat and the posterior nares. In cases of pneumonia, of course, we know that the pneumococci are present in abundance in the exudate, and it is easily conceivable that from here they may be distributed upward over the bronchial and tracheal mucosa, and that during the act of coughing and expectoration the larynx, pharynx and mouth of the individual also become contaminated. This, however, raises the question whether pneumonia is not a descending infection, which is the view that is now generally held. But in that case we would have a right to assume that every pneumonic was for a while a passive carrier until a sufficient number of organisms became available to bring about such a complete overthrow of the natural defences as to render an infection of the lung possible. And in that case the question, where does this initial development take place, still remains unanswered. But supposing even that the infection were an ascending one, it is more than likely that the primary focus is nevertheless located in the upper respiratory tract. In the healthy carrier, of course, there is no reason for assuming that the organisms come from the deeper portion of the respiratory tract. In the absence of definite information on the subject we can only surmise that in the pneumococcus carriers also the crevices of the lymphatic structures of the upper respiratory tract contain foci in which the organisms find suitable conditions for their development, and from which they find their way to the surface and into the saliva. The fact that they are so frequently present in the latter, in which the diphtheria bacillus and the meningococcus are only exceptionally found, would further suggest that they might develop in diseased areas about the teeth. Streptococci are here so constantly met with that it would not be at all surprising if pneumococci also here found

conditions favorable for their growth. Dochez, Avery and Stillman when speaking of their findings in individuals who *were* not or had not been suffering from pneumonia quite constantly refer to "normal mouths." But every one knows that relatively few mouths are normal, and from the standpoint of the epidemiology of lobar pneumonia it would seem most important to ascertain whether or not pneumococcus carriers actually do have normal "mouths," which would, of course, include the condition of the teeth. A systematic investigation in this direction would suggest itself as a most promising field for future investigation.

Mode of Infection.—Regarding the manner in which the pneumonia patient produces carriers, and these in turn infect others, we are, of course, most liable to think of a direct transfer of the organisms through sputum spray: While this no doubt can occur, there is reason for believing that infection may also take place through the dust of rooms in which patients or carriers live or have lived. Recent investigations in connection with the dissemination of streptococci, even in cubicle wards, have shown how readily this can occur when all other channels for the transfer have practically been eliminated and air currents and dust remained as the only possible factors.¹² Stillman¹³ has investigated this possibility in connection with the types of pneumonia that we are considering and obtained results which speak for themselves.

TYPE ANALYSIS OF DUST OBTAINED FROM ROOMS.

	No. of rooms (a).	Percentages of positive findings.	No. of rooms (b).	Percentages of positive findings.
Type I	1	5.5	25	33.78
" II	0	0.0	23	31.08
" II a	0	0.0	0	0.0
" II b	4	22.0	2	2.7
" II x	3	16.6	2	2.7
" III	2	11.0	2	2.7
" IV	8	44.4	20	27.02
<hr/>				
Pneumococci present in . . .	18	29.0	74	40.0
" absent in	44	71.0	109	59.6
<hr/>				
	62		183	

a, in which no pneumonia had occurred; b, in which pneumonia had occurred.

The fact that a pneumococcus of type I was found in a single instance in a house in which no pneumonia had occurred can, of course, be no more surprising than the occasional finding of the same type or type II in the mouth of a person giving no history of contact with pneumonia. For so long as we recognize the existence of carriers we must also be prepared to find secondary carriers resulting through contact with primary ones, and such persons would naturally give no history of contact, but could cause a dissemination of the organisms in their surroundings.

Stillman also found that, as a rule, the dust became negative before the carriers, living in the same household in which a case of pneumonia of type I or II had occurred. But in two instances the dust remained positive longer than the carriers. The most persistently positive dust was gotten from two homes in which the most persistent carriers lived. In one of these (type I) the dust was positive for fifty days while the carrier had not become negative at the end of eighty days. In the other (type II) the carrier was still positive at the end of seventy days and the dust on the fifty-seventh. We may conclude that there is good reason to believe that both patient and carrier may infect others not only directly, but also indirectly through pneumococcus-laden dust, and it would seem as though the latter method were indeed the more likely. This observation in no way detracts from the importance of the carrier as a factor in the dissemination of the disease. He is a menace to the community because he contaminates the air, while the typhoid carrier is a menace because he contaminates the food and drink.

Examples Illustrating the Role of Pneumococcus Carriers in the Dissemination of the Disease.—As yet but little work has been done with the view of demonstrating in a concrete manner the relationship between actual cases of lobar pneumonia and carriers. Bearing in mind the relatively brief duration of the carrier period, the mobility of the individual and the possibility—indeed, the likelihood—that he may bring about the dissemination of the disease through infection of the dust of rooms in which he may have lived for

only a short time, it will be realized that not every case of pneumonia will lend itself to a fruitful investigation of its origin. In large communities such an investigation will perhaps only exceptionally be a profitable one. A few well-chosen instances, however, properly studied, will suffice for our purposes. Stillman has related several examples which practically leave no doubt that the carrier of pneumococci of the types we have been considering in reality does play the role which Dochez and Avery's work has suggested. One instance which seems especially suggestive is the following:¹⁴ "A patient was admitted to the hospital suffering from pneumonia due to pneumococcus, type I. Specimens of sputum were obtained from the other members of the household. One five-year-old daughter was found to be a type I carrier; the other two members of the household were negative. The dust of the room which the patient had previously occupied in this house also showed a type I pneumococcus. The little girl was sent to board with friends while her mother was in the hospital. She spent three days with the first family and then went to visit in the Bronx. Six days after she left, a child in the home where she had visited came down with pneumonia, due to pneumococcus type I. Specimens of sputum from the other members of this household were negative, but from the dust in the sick child's room a pneumococcus of type I was isolated. At the home in the Bronx where the little girl visited for ten days no case of pneumonia developed and the sputum of the members of this family as well as the dust failed to show the presence of pneumococcus type I. The child next went to visit friends in Brooklyn. Although the sputa from the members of this household were negative, from the dust a type I pneumococcus was recovered."

Quite instructive also is the following case: A patient who had just recovered from a type I pneumonia left the hospital March 9. The next day he went to see his brother who had developed a type II pneumonia. On March 12 the same individual who had just recovered from the type I infection developed a pneumonia due to a type II pneumococcus.

An interesting contribution to the epidemiology of pneumonia, based upon type determination, has also been made by Sydenstricker and Sutton,²⁵ and is here given as originally reported.

Sparrows Point is the home of the Maryland Division of the Bethlehem Steel Company. It is situated on the waterfront near the mouth of the Patapsco River, about 10 miles below Baltimore. The plant employs about 7000 men. Some have homes in Baltimore, but the majority live in the town which has grown up around the plant. About 2000 of the men are negroes. Half of these live in the company's shanties, in a section of the works called "Coke Oven Row." This group of shanties is shown in Fig. 3, which is reproduced from the company's map with their consent. The shanties are built ten in a row. Each accommodates four men. The shanty is a small room fourteen feet square, with four bunks, four lockers, a washstand and a stove. One building is used as a store, barber-shop and pool-room. This is a common meeting-place, and usually crowded. Most of the men get their own meals, but there is a cook-shop which some of the men use.

Formerly all the shanties were frame buildings, the wall being a single thickness of board. Recently a group of 100 tile and concrete shanties has been added. The shanty group is situated directly on the shore, and is consequently exposed to all sorts of weather. The majority of our pneumonia cases came from this Coke Oven group. The view commonly held among the company's physicians is that pneumonia has always had a high incidence and been of a severe form among these men in the shanties.

The group seems to offer excellent opportunities for epidemiological studies. It is an isolated group of 1000 men living under almost identical conditions. They are in intimate contact with each other and with no one else. They crowd into the store or into each other's shanties. They frequently close the two small windows and door, and, in addition, try to pack the cracks between the boards with newspaper, especially in winter, to keep out the cold. They sleep sometimes with the stove lit, or, if too tired to start a

fire, they sleep without it, often with too few blankets. Thus these men are exposed to sudden changes of temperature. Few of them, however, are exposed to the heat of the furnaces, since practically all are employed on outside work. Another factor, which may play a role in their susceptibility, is that

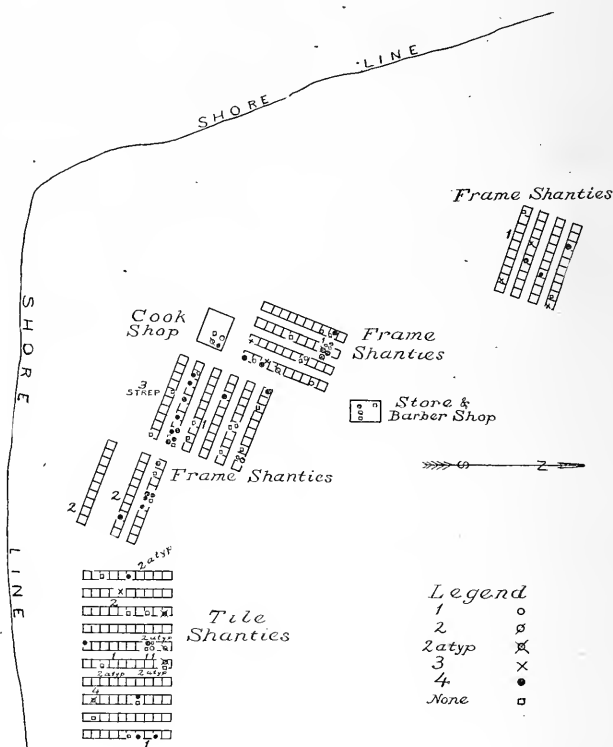


FIG 3.

most of them come from the south and are not used to winters as severe as in this climate.

It is this group, then, that we undertook to study. We collected, during the latter part of January, specimens of sputum from 100 of these men. In Fig. 3 the types are spotted on their respective shanties. The figures by the

shanties give the types of the cases of pneumonia from each shanty which were treated in the hospital.

Of the four men employed in the cook-shop, one carried a type I, one a type II, the other a type IV, and one was free from pneumococci.

The sputa were collected in sterile bottles, brought immediately to the laboratory and white mice then inoculated with 0.5 c.c. of sputum subcutaneously. The mice were allowed to die and cultures made from the peritoneum and from the heart's blood. The pneumococci were usually obtained in pure culture.

In order to have a normal group with which to compare them, we cultured in a similar way 50 sputa collected at random among our dispensary patients. The results of these studies are tabulated in Table III. The striking difference is in the high incidence of the fixed types on the Coke Oven group—the number of type IV pneumococci is practically the same, the difference being in the small number of negative cultures in the Sparrows Point group. The high incidence of fixed types among the mouth organisms parallels the high percentage of fixed-type pneumonias and the extremely low percentage of cases due to the type IV pneumococcus among Coke Oven Row cases, as contrasted with our city cases of pneumonia in Table IV. Another point is a pneumonia morbidity rate at Coke Oven Row of approximately 6 per cent., which is very high in comparison with the Health Department rate for Baltimore City of less than 0.5 per cent. The latter is an estimate based on the Health Department mortality rate. The mortality of the Sparrows Point group is shown in Table V. It varies little from the rates given for the entire group.

Several interesting features warrant special mention. In Shanty 609 we collected sputa from six men. Two contained atypical type II pneumococci, one a type IV and three yielded no pneumococci. One of the last group later developed a type I pneumonia. In Shanty 43 all four men developed pneumonia the same day, following a sudden fall in temperature. One was treated in another hospital in this city. The type of pneumococcus was not determined in this case. One refused hospital care and went to his home in the south.

The other two came here. They had type I and atypical type II infections, respectively. They stayed together in a side room by themselves the entire time. The one that was recovering from the atypical type II infection suddenly relapsed after his temperature had become normal. A lobe in the opposite lung from the one previously involved became consolidated. His blood cultures again became positive. This time a type I pneumococcus was isolated. Prior to the isolation of the type I organism, the development in the patient's serum of antibodies active toward the atypical type II strain suggested that we would find that the new consolidation was due to a pneumococcus of an entirely different strain. This patient received antipneumococcus (type I) serum and made an uneventful recovery except for a moderate serum sickness. If he contracted the type I infection from his shanty-mate in the hospital, it is interesting that he contracted a different type in the shanty.

Summary.—Examination of 100 specimens of sputum from healthy negroes living in the shanties of the Bethlehem Steel Works showed 22 per cent. of pneumococci belonging to fixed types in contrast to 6 per cent. of a group of our dispensary patients. The number of the ordinary saprophytic type IV organisms was practically identical in the two groups. The increase in the fixed types was at the expense of the group that do not harbor pneumococci in their mouths. This high percentage of healthy individuals carrying pneumococci of fixed types in their mouths occurred in a community where the percentage of cases of lobar pneumonia due to organisms of fixed types was likewise very high.

TABLE I.—SUMMARY OF CASES.

Type.	Black.		White.		Total.
	Living.	Dead.	Living.	Dead.	
I	12	6	3	3	24
II	3	0	1	0	4
II (atypical)	7	4	0	1	12
IV	15	2	3	2	22
Ungrouped	1	1	0	0	2
<i>Streptococcus mucosus</i>	1	0	0	0	1
Friedländer's bacillus	0	0	0	1	1
Total	39	13	7	7	66

TABLE II.—MORTALITY RATES.

Type.	Black. Per cent.	White. Per cent.	Mixed. Per cent.
I	33.3	50	41.7
II	0.0	0	0
II (atypical)	36.3	100	41.6
IV	11.8	40	18.2
Mixed	25.0	50	30.3

} 31.3

TABLE III.—PNEUMOCOCCI ISOLATED FROM MOUTHS OF
HEALTHY INDIVIDUALS.

Type.	Sparrows Point (100 cases). Per cent.	Dispensary (50 cases). Per cent.
I	6	0
II	6	2
II (atypical)	4	2
III	6	2
IV	35	32
None	43	62
	<hr/> 100	<hr/> 100

} 22

} 6

Other examples of a convincing character will, no doubt, soon become available now that the mode of transmission of the more dangerous types of respiratory infections is being studied with such care in our army camps, but the few instances just related suffice to show that the danger from the pneumococcus carrier is a very real one.

The Recognition of the Pneumococcus Carriers.—The recognition of pneumococcus carriers of the types which we have been considering in the foregoing pages involves two essential steps: viz., the isolation of the organism in pure culture and the study of its behavior toward agglutinating or precipitating antisera.

Isolation of the Organism.—Owing to the fact that in carrier studies sputum, properly speaking, is usually not available, some of the simpler methods of investigation which furnish such excellent results in type determination in actual cases of pneumonia can unfortunately be used only in part. The material with which we are obliged to work is either a swab specimen from the throat or a sample of saliva, and as contaminating organisms cannot here be removed by any

mechanical method it is necessary to inoculate white mice in order to obtain pure cultures. This is time-consuming and calls for a large number of animals, but cannot be avoided.

A few drops of saliva (0.2 to 0.3 c.c.), which should be collected in a sterile bottle and taken to the laboratory at once, are injected intraperitoneally into mice. The animals are killed the next morning, if they survive until then, when cultures and smears are made from the peritoneal cavity and the heart's blood under aseptic precautions.

For cultural purposes a special glucose-blood broth is employed as recommended by Avery.¹⁵ This is a meat-infusion broth, 0.3 to 0.5 per cent. acid to phenolphthalein, to which the requisite amount of glucose solution and of blood is added when needed, the three components being meanwhile kept separately in the ice-box, as suggested by Vaughan.¹⁶ The broth is conveniently put up in lots of 100 c.c. each and sterilized on three consecutive days, for twenty minutes at a time, in an Arnold steam sterilizer. The glucose solution is one of 20 per cent. and conveniently prepared by autoclaving distilled water in 50 c.c. lots., and then adding 10 grams of chemically pure glucose to each lot, which is subsequently sterilized by boiling.

Sterile defibrinated blood may be obtained, as suggested by Vaughan, by withdrawing from 20 to 30 c.c. of blood from an arm vein of a normal subject, or at any rate from one not suffering from a bacterial infection, and placing this in a sterile bottle containing some sterile glass beads. The blood is immediately shaken and then kept on ice.

I have found it convenient to use sterile blood sent in for Wassermann examination for work of this kind. But little is really needed for the Wassermann test, and the remainder I stir up with a sterile glass rod and then transfer the liberated corpuscles together with the serum to a small flask, which is placed on ice.

In the absence of human blood rabbit blood may be used.

Immediately before use small test-tubes are then charged with 5 c.c. of broth and 0.25 c.c. of glucose solution and of blood each, so that the final product contains 1 per cent. glucose and 5 per cent. of blood.

One or more tubes of this culture medium are inoculated from the peritoneal cavity and the heart blood of the infected mouse and then incubated at 37°C ., overnight. At the same time it is advisable to smear a blood-agar plate directly—partly with the peritoneal fluid, partly with the mouse's heart blood, so that the pneumococcus may be obtained in pure culture, should other organisms be present at the same time.

A direct examination of suitably stained smears will usually indicate at once whether other organisms are present besides capsulated diplococci, for which we are in search. The following day we may then proceed with the examination of the cultures that have been obtained in the special medium, providing that microscopic examination has shown that no other organisms are present. Otherwise subcultures will have to be prepared from the blood agar plates, in the same medium, and allowed to grow out. If the culture is pure the tube is centrifugalized for a couple of minutes at low speed to throw down the red cells, when the supernatant fluid may be subjected either to the precipitation or the agglutination test as follows:

Precipitin Test.—The turbid bacterial emulsion is transferred to a tube containing 1 c.c. of sterile ox bile and incubated at 37°C . for about twenty minutes. If the culture was pure the turbidity will clear up, owing to the dissolution of the pneumococci in the bile. If it has not cleared entirely the specimen is centrifugalized at high speed until every trace of turbidity has disappeared. A series of small tubes is now charged with 0.5 c.c. each of the cleared culture and the corresponding antisera. Type I serum is best used undiluted, as is also type II serum, while type III is diluted 1 in 5. The results may be read in a few minutes and are sharp and distinct, a turbidity resulting in the tube which contains the antiserum corresponding to the type present. Should a positive reaction be obtained with type II serum an additional specimen is put up with a 1 to 10 dilution of this serum. If now a negative reaction is obtained the inference is that the type was an atypical II while a positive reaction indicates type II proper. The presence of type IV is indicated if a negative result is obtained with all three of the antisera.

Instead of working with a culture of the organisms as just described, Blake suggests to wash out the peritoneal exudate from the mouse with 4 to 5 c.c. of sterile saline, and after centrifugation to use the clear supernatant fluid.²³

It has been suggested that type I, II or III may be associated with type IV in a person's mouth and that the presence of the latter may obscure that of any one of the fixed types in the final test. But, as a matter of fact, there is no danger of confusion from this source if a mouse is used to begin with, as it has been conclusively established that in the body of the latter the dangerous types rapidly outgrow the less pathogenic type IV.

Agglutination Test.—The agglutination test is performed in the same manner as the precipitation test, barring the use of bile, of course. After slowly centrifugalizing the culture, so as to throw down the red cells, but not the bacteria (two to five minutes at slow speed) the supernatant emulsion is pipetted off and placed in 0.5 c.c. portions in small tubes as above. The antisera are then added, well mixed with the emulsion, and the tubes placed in the incubator for about two hours. Agglutination is usually well defined already at the end of an hour, and one can then readily pick out the types by noting the tube in which the supernatant fluid is clearer than in the others. On shaking, moreover, it will be noted that the bacteria have gathered in fairly large floculi in the positive tube, while in the negative specimens this does not occur. At the end of two hours the specimens are taken out of the incubator and may be allowed to stand at room temperature for a while longer. In the absence of contaminating organisms the readings are then sharp and distinct. I have found it convenient to put up a fourth tube and to add to this 0.5 c.c. of a 10 per cent. solution of sodium taurocholate. The clearing of this serves as additional proof that we are actually dealing with the pneumococcus.

Should a positive reaction be gotten with undiluted type II serum an additional specimen is put up with the same serum, diluted 1 to 10, and as in the case of the precipitin reaction, an atypical type II may be inferred if agglutination now does not occur, while this will take place, of course, in the presence

of type II proper. As in the precipitin test, antiserum I is used undiluted, and serum III diluted 1 in 5.

Type Determination in Sputa.—If for any reason it should be desired to study types of pneumococci in a sputum coming from the lung, the same method may be employed as described above, or we may resort to the abbreviated method of Avery-Vaughan, which will furnish a positive result within a day. The prerequisite of success is that the sputum actually does come from the lung. Unless this is assured the abbreviated method is not applicable, and in such a case the initial isolation of the pneumococci must be conducted with the aid of the mouse. *To secure a proper specimen of sputum* it is recommended to collect what is first coughed up on awaking and after rinsing the mouth with sterile saline. In the case of a pneumonia patient it will be found that a fit of coughing will be started if he attempts to lie on his unaffected side. This usually terminates in the expectoration of one mass of sputum, which is quite sufficient for examination. The specimen is immediately brought to the laboratory and placed in the ice-box if it cannot be examined at once, which latter is preferable, as the sputa are very apt to undergo autolysis even in the ice-box. The thickest portion of the sputum is then taken and a kernel, the size of a bean, washed in three or four changes of sterile saline in sterile dishes. The specimen is then transferred to a tube of blood-glucose-bouillon (prepared as described above), taking care that it does not adhere to the sides of the tube, but is immersed altogether in the culture fluid. Avery recommends that the specimen after washing be first ground in a small sterile mortar with 0.5 to 1 c.c. of broth and then transferred to the culture tube. This, however, is not necessary and is inconvenient if a number of specimens are to be examined at one time.

The specimen is then incubated for five hours in a water-bath at 37° C., at the expiration of which time a sufficiently rich emulsion of organisms is usually available to conduct either the precipitin or the agglutination test as one desires. At the same time streak cultures are made on blood-agar in order to secure absolutely pure cultures, with which the

requisite tests can be repeated if this is thought to be desirable.

The precipitin test and the agglutination test are conducted as described above, preference being given the former if the cultures on microscopic examination are found to contain other organisms besides pneumococci.

Contamination with saliva or the secretions from the pharynx or posterior nares is, of course, very apt to give rise to erroneous results, and lead to a type IV diagnosis when the organism in the deeper air passages was in reality of a different type. In the *artificial mouse*, as the culture medium of Avery has been termed, the different types would, of course, grow side by side, and it is hence desirable before diagnosing type IV either to repeat the examination with a specimen of sputum that has been selected with special care, or to resort to mouse inoculation.

*Krumwiede's Method.*²⁴—This is based upon the extraction with saline of the precipitable substance contained in the pneumococci in sputum after coagulation of the associated albumins, which is then followed by the application of the precipitin test to the extract. The advantages claimed for the method are its simplicity and the fact that, given a proper specimen of sputum, a determination of the type can be made in one-half to one hour after the receipt of the specimen. For carrier diagnosis the method is, however, not applicable, as the sputum specimens which can be secured from convalescent pneumonia patients and passive carriers never contain pneumococci in sufficient numbers to yield an antigen directly that would be strong enough to give a visible reaction with the corresponding antisera. It may serve, however, for determining the type of the infection during the active period of the malady. Its limitations are the same as those which apply to the precipitation method as described above. In doubtful cases it should be supplemented by Avery's method or by the animal experiment.

Technic.—From 3 to 10 c.c. of the sputum, depending on the amount available, are poured from the sputum container into a test-tube. This is placed in boiling water for several minutes or longer until a more or less firm coagulum results,

which will occur if the specimen is a suitable one. The coagulum is then broken up with a heavy platinum wire or glass rod, and saline is added. Just enough saline should be added so that, on subsequent centrifuging, there will be sufficient fluid to carry out the test. If too much is added, the resulting antigen may be too dilute. In some instances little or no saline is necessary, as sufficient fluid separates from the coagulum.

After the addition of the saline, the tube is again placed in boiling water for a few minutes to extract the soluble antigen from the coagulum, the tube being shaken several times during the heating. The broken clot is then thrown down by centrifuge, and the clear supernatant fluid used for the test. To hasten the appearance of the reaction and to obtain a reaction even should the antigen be dilute, we layer the antigen over the "type" serums, using the latter undiluted. Two-tenths c.c. of the three "type" serums are placed in narrow test-tubes, and the antigen added from a capillary tube with a rubber teat. If the tubes containing the serum are tilted and the antigen dropped slowly on the side of the tube just above the serum, no difficulty will be encountered in obtaining sharp layers, as the undiluted serum is sufficiently higher in its specific gravity. The tubes are then placed in the water-bath at from 50° to 55° C. and observed after several minutes.

If a fixed type was present in the sputum, and should the sputum have been rich in antigen, a definite contact ring is seen in the tube containing the homologous serum. With sputums less rich in antigen, the ring may develop more slowly, and it will be less marked. Some experience is necessary in detecting the less marked contact rings and in differentiating them from an apparent ring which may be confusing, if one of the serums is darker in color, giving thus a sharper contrast with the supernatant antigen. The true ring is more or less opaque, and this quality can be seen by tilting the tubes and looking at the area of contact against a dark background; for example, the lower edge of a dark shade raised to just above the level of the eyes. The advantage of the ring test is that a ring may be evident, whereas

definite clouding or a visible precipitate may appear only after longer incubation, or may be so slight even after an hour's incubation as to leave one in doubt. It is well to shake the tubes after twenty minutes, as many of the specimens will show definite clouding or precipitates either at once or on further incubation, thus checking the ring reading. The final reading may be made in from ten minutes to one-half hour.

Management of the Pneumococcus Carrier.—*Quarantine.*—As the passive pneumococcus carrier owes his fatal gift to the active carrier, it is clear that the management of the carrier problem must begin at the bedside of the patient. The latter should be isolated so far as possible from the remaining members of the household, and in a hospital, from the other patients of the ward. Special pneumococcus wards would seem to be indicated only if the types could be kept apart. Theoretically it would seem best to have a receiving ward in which the patient should be placed until the type of his pneumonia has been ascertained, and then to move him into a corresponding ward. Such an arrangement would suggest itself as a rational one for our military hospitals, where fairly large numbers of cases are likely to occur and where the danger from carriers is even greater than in civil communities.

As it is scarcely possible to prevent sputum spray from the patient to become disseminated in his immediate surroundings, and as the dust in the patient's room probably is more dangerous than immediate contact with the patient, a *face mask* should be worn by all those who have to do with his care.¹⁷ Such a mask is now used in our military hospitals as a matter of routine, and will probably prove the most important single factor in preventing the development of carriers. For the same reason the liberal use of disinfectants would seem to be indicated in the sick room or ward, which in turn would mean that these be stripped of everything in the nature of hangings and carpets and in fact all non-essentials. The management of a patient along these lines is, of course, impossible in small quarters, and for this reason, if no other, the individual should be cared for in a hospital, the home

being in the meantime disinfected by the proper authorities. It is high time that people should realize that no progress in the eradication of this, the most fatal of our common acute infectious diseases, is possible unless suitable health laws be enacted and *carried out*. At present the activity of most health departments in our country amounts to *nil*, so far as the effective control of the disease in question is concerned. Up to the time of writing not a single law or ordinance has been enacted, so far as I have been able to ascertain, beyond the mere reporting of the cases—which itself is only called for here and there—which could in any sense be regarded as a definite step looking toward the conquest or even the partial control of pneumonia. So long as bacteriological examinations of pneumonia cases and their contacts are not made as a matter of routine; so long as adequate hospital facilities do not exist for their management; so long as pneumonia convalescents are allowed to mingle with others irrespective of the fact that they may be carriers; so long as the carriers are not located and at least instructed regarding the menace which they represent to others, so long will pneumonia not only remain with us, but, to judge from present indications, will become an increasing menace as time goes on. It is perfectly clear from the work that has been done in our military hospitals that pneumonia is a disease that can be successfully combated, and unless similar efforts are promptly made by the health authorities of our civil communities it is high time that these should be gotten rid of and replaced by men who are efficient and who are capable and willing to perform those duties for which they are appointed. The first and most important step in this direction is the removal of all health departments from political control.

As I have just indicated, suitable *bacteriological control of pneumonia convalescents, contacts and resultant healthy carriers*, will prove to be the *sine qua non* in any attempt to diminish the spread of pneumonia. Fortunately we are now in the possession of a practical technic for this purpose, and no time should be lost in putting to practical use our ability to recognize pneumonia carriers of the most dangerous types at any rate.

As the pneumococcus carrier, whether active or passive, is of peculiar danger to others, owing to the probable manner in which he infects, stricter rules will be necessary for his control than for typhoid carriers, for example, or even for diphtheria carriers, for here we at least have an effective antiserum with which to control the disease when once it has developed, whereas in connection with pneumonia we stand powerless before types II and III, and even with regard to type I its treatment with antiserum has not yet proved so satisfactory as to merit being called a curative one.

For these reasons it is desirable that all individuals harboring pneumococci of types I and II at any rate should either be quarantined altogether or their movements restricted in such a manner that they cannot endanger the lives of others. A coughing carrier should not be permitted to scatter his germs broadcast, to use the same drinking utensils and tableware as others, to sleep in the same room or even in the same bed with others, to shake out his pocket handkerchief before proceeding to a sonorous emptying of his nose. But even the non-coughing carrier can hardly be regarded as a suitable companion or visitor for those who are naturally more prone to develop pneumonia than others, such as the aged and infirm, young children, patients suffering or convalescent from other diseases, from operations and the like.

Disinfection of Carriers.—Whether or not it is possible by medicinal means to prevent the development of the carrier state, or to shorten or to arrest it, when once it has become established, is not known. To judge from the failure of all such attempts in connection with carriers of other bacteria, the outlook is not promising. If the pneumococci were present only on the mucous surfaces of the upper respiratory tract or in the saliva, one might expect some good from the use of mouth washes and gargles, containing ingredients that have a definite pneumococcidal effect in the test-tube, such as ethyl hydrocuprein and other cinchonics, as has been suggested by Kolmer and Steinfeld.¹⁸ If, however, their proper habitat is in the deeper structures it is evident that the infinitesimal quantities of these substances which would come in contact only with those organisms that have found their

way to the free surfaces could hardly be effective. Kolmer and Steinfeld have thus far not tested their suggested method of treatment in actual cases, and merely recommended it on the basis of the well-known pneumococcidal activity of the cinchonics in the test-tube. The formula proposed for washing the mouth and gargling is the following:

Ethyl hydrocuprein hydrochlorid, or quinine bisulphate	0.005
Liquor thymolis*	5.0
Aqua distillata ad	50.0

A similar solution made up in undiluted Dobell's solution is suggested for douching or spraying the nose, or the substance may be incorporated in a dental cream and used for cleansing the teeth.

Management of carriers of Types III and IV.—While the foregoing remarks apply, of course, with special force to carriers of the two types of pneumococci, which are met with practically only in active cases or their contacts, and which we have reason to look upon as purely parasitic types, viz., I and II, according to Dochez's classification, any pneumonia patient harboring type III should be treated and viewed in the same manner. But as type III evidently also occurs in a fair percentage of healthy individuals who have not all, at any rate, been in contact with corresponding active cases, and probably represents an organism which is facultatively parasitic or saprophytic, the question arises whether healthy carriers of this type also should be subjected to the same rigid regulations which we regard as imperative in the management of types I and II. On the face of it this would indeed be impossible, as the number is far too large, and as there could be but little object in quarantining only the occasional case that we would meet with more or less accidentally. Bearing in mind, however, that this type, when it does produce pneumonia, is responsible for the highest death-rate, *i. e.*, some 60 per cent., it stands to reason that an attitude

* The liquor thymolis has the following composition: Benzoic acid, 64 grains; boric acid, 128 grains; thymol and menthol, ãã 16 grains; oil of eucalyptus, of wintergreen and monarda, ãã 4 drops; alcohol and glycerine, ãã 4 ounces; water sufficient to make up 16 ounces.

of indifference toward such carriers is scarcely warrantable. The least that we can do is to keep such carriers under a certain supervision and to instruct them how to avoid, so far as possible, the infection of others. Steps should further be taken to study thoroughly the extent to which this organism is found in human beings and their environment, with a view of obtaining a possible clue to their relatively frequent presence in the mouths of apparently healthy individuals and to determine whether indeed they are facultative parasites only.

As regards type IV carriers, our knowledge is as yet too meager to warrant the laying down of any rules in reference to their management. Type IV, as I have pointed out, is represented by a heterogeneous lot of pneumococci, differing from the so-called fixed types, and is regarded as essentially a saprophyte, which can readily exist in the mouth of practically any person, and which when it does cause pneumonia produces a relatively mild form of the disease. That this type also *may* at times become dangerous has, however, been abundantly demonstrated during the present epidemic of so-called influenza, where a considerable percentage of the complicating pneumonias with a high death rate has been found to be due to pneumococci of this order. As has been suggested, it is possible that these cases are really auto-descending infections, the path for their downward course having perhaps been opened by some other organism. If this view is correct, individuals harboring this type cannot be regarded as carriers in the sense in which the term is now generally used. They may be dangerous to themselves, but they are not dangerous to others. Whether this view is correct, however, remains to be seen.

Protective Inoculation Against the Pneumococcus.—In view of the manifest difficulties which stand in the way of a successful control of pneumococcus carriers by quarantine, or their disinfection by therapeutic means, it is particularly gratifying to note that a certain degree of protection, at any rate, can be secured against pneumococcus infections by inoculation with a corresponding vaccine. While it is hardly to be expected that sterilization of the carrier can be effected in

this manner, it is clear that a diminution in the incidence of the disease must in turn lead to a diminution in the number of carriers and that the desired result will thus be indirectly achieved. Experiments in this direction were first undertaken on a large scale by Sir Almroth Wright¹⁹ in South Africa, in 1911 and 1912, among native workers in the mines. The results obtained at the Premier Mine were very encouraging, as the death-rate among 17,000 inoculated men was only 6.89 per thousand, whereas among 6700 non-inoculated controls it was 17.72, both sets having been selected entirely at random. On the Rand, on the other hand, no material difference was noted between the two classes.²⁰ This incongruity in the results Darling²¹ attributed to the possibility that the vaccine used at the Premier Mine was made up from a different strain from that used on the Rand. As a matter of fact, nothing definite was known of the existence of different strains of pneumococci at that time, and it is interesting to note that Darling's prophetic suggestion has since been supplied with the necessary experimental basis. For, as we have seen, in 1913 Dochez and Gillespie, in the United States, and Lister,²² in South Africa, showed that different strains of pneumococci actually do exist, and shortly after, the latter undertook active immunization of the workers in three large mines on this basis. The results were such as to leave no doubt that protection can be afforded in this manner, for it was found not only that there was a definite decrease in the incidence and mortality from pneumonia, but—and most important of all—that the diminution in the incidence corresponded to the type of the vaccine which was employed. At the Crown Mines no cases of the types against which the men had been vaccinated thus occurred during the nine months of observation. In commenting upon the value of inoculation of a large body of people in a community, Lister* very properly points out that in consequence of the lowered incidence of the disease the number of carriers also must be diminished, and that the non-inoculated portion of the community thus benefits as a result.

* In preparing his vaccine Lister killed the organisms by the use of germicides, and not by heat. Three subcutaneous injections were given, each dose containing from seven to ten million cocci.

In the United States vaccination against the pneumococcus on a large scale was first undertaken during the early part of the winter of 1917-18, when 12,519 men were vaccinated at Camp Upton. The results have been reported by Cecil and Austin.²³ The vaccine itself was made up from strains I, II and III. The inoculations were made subcutaneously at intervals of five to seven days, 3,000,000,000 (one of each kind) being given the first time, 6,000,000,000 (2 of each) the second time, 7,500,000,000 (3 each of types I and II and $1\frac{1}{2}$ of type III) the third time and the same dose the fourth time. The great majority of the men received three or four injections. The subsequent observation period unfortunately covers only ten weeks, but even during this short time a marked difference in the pneumococcus pneumonia incidence is discernible between the vaccinated and the non-vaccinated groups, which latter numbered 19,481. Among the vaccinated men there occurred but a single case of type pneumonia (I), and as this developed twenty-four hours after the first injection, it is reasonable to conclude that infection had already occurred before that time and that the case may therefore be eliminated. Among the non-vaccinated men, on the other hand, there occurred 26 cases of type pneumonia.

It is interesting to note that the vaccination apparently also had a protective effect against type IV, for whereas only 6 cases of this order developed among the men who had received two or more injections (0.04 per cent.), there were 33 among the controls (0.2 per cent.), giving a ratio of 1 to 5. While 6 of the 33, moreover, died (18 per cent.), all of the vaccinated men, recovered.

Evidently there was a considerable degree of cross-protection, which is interesting in itself, but even more remarkable is the fact that the vaccination afforded a marked protection against streptococcus pneumonia which was prevalent at the same time. The results which were here obtained will be discussed in the section on Streptococcus Carriers.

The findings obtained at Camp Upton, by themselves, are, of course, too few to warrant any far-reaching conclusions, but taken in conjunction with those reported by Lister from South Africa they clearly indicate that at last a very

definite advance has been made toward the conquest of this scourge than which none is more formidable in civilized lands.¹

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¹ During the recent epidemic of so-called influenza the United States Army made use of a triple pneumococcus vaccine on a large scale for prophylactic purposes, in view of the fact that most of the fatalities from the disease were due to the action of pneumococci, but up to the time of writing no data are available from which conclusions can be drawn.

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STREPTOCOCCUS INFECTIONS.

CAMP SEPTICEMIA, BRONCHOPNEUMONIA, SEPTIC SORE
THROAT, PUERPERAL FEVER, ETC.

THE question as to whether or not the forms of streptococcus infection, and more particularly those which have a tendency to appear in epidemic form, such as our common winter colds or gripes, are disseminated by human carriers of the type which we are principally considering in these pages has until recently been largely a matter of conjecture. The principal difficulty which has stood in the way of a satisfactory solution of the problem has been our inability to differentiate those organisms belonging to the streptococcus family, which are met with in the corresponding lesions from the streptococci which may be cultivated from supposedly any so-called normal individual's throat or mouth. We have tacitly and, no doubt, properly assumed that a streptococcus which we meet with in an acutely inflamed antrum, or middle ear, or mastoid, or in deposits on acutely inflamed tonsils, or as the predominating organism in the sputum of cases of bronchitis or in connection with the bronchopneumonia of old people, is the organism that is actually responsible for the associated lesions. But unfortunately we have not been able to state when finding apparently identical organisms in the throats of healthy individuals whether these were in reality identical with the former, and it is clear that unless we are able to prove this identity we have no right to assume it, and we could not accordingly declare that this or that person is a carrier of a type of streptococcus that under suitable conditions is capable of producing a certain clinical or pathological anatomical picture. So long as we were unaware of the existence of distinct types of pneumococci and their exclusive occurrence in certain cases of lobar pneumonia dur-

ing the active stage and the convalescence from the disease, and in individuals who have been in more or less intimate contact with such cases, we could not rightfully speak of pneumococcus carriers in the sense in which the term is now employed. It was long known that pneumococci exist in the mouths of from 50 to 80 per cent. of healthy individuals, and it was assumed that when pneumonia did develop it was essentially an auto-infection, but the proof that the latter is not the case in the majority of cases could only be furnished when we had come to recognize that different types of pneumonia exist and to learn to differentiate these from each other. For the assumption that the disease was largely disseminated by carriers there was formerly, indeed, very little epidemiological evidence, as contact cases of pneumococcus pneumonia are after all infrequent.

In the case of the streptococcus infections, on the other hand, to which I have referred above and which occur with such constancy winter after winter, we have sufficient circumstantial evidence to assume that their dissemination takes place either through direct or indirect contact. But, as I have said before, we have unfortunately not been able to furnish the requisite bacteriological proof, owing to our inability to distinguish between pathogenic and non-pathogenic types, if indeed there be such types, and the pathogenic properties be not of a temporary nature only. It is true we recognize a *Streptococcus viridans*, a *Streptococcus hemolyticus* and a *Streptococcus mucosus*, but in view of our lack of knowledge concerning their pathogenicity and their frequent occurrence in the throats of healthy individuals we have not been in a position where we could designate anyone harboring these organisms as a carrier, meaning thereby a potential disease-producing agent. We know that a *Streptococcus viridans* has a special affinity for serous membranes, that a *Streptococcus mucosus* has a tendency to invade lymphatic structures and that a *Streptococcus hemolyticus* is frequently found in connection with "grippal" bronchitis and "grippal" pneumonia, but, as I have said before, we do not know whether these particular types are identical with those encountered in the throats of healthy persons.

Camp Septicemia and Bronchopneumonia.—Our knowledge of these matters has, however, been greatly increased through the splendid series of studies that have been carried on during the winter of 1917–1918 in connection with the epidemic of streptococcus infections and notably of streptococcus pneumonias which occurred in certain camps of our national army. The course of this epidemic and its relation to carriers was practically the same in all cases, and is well exemplified by the experience gathered at Camp Zachary Taylor, Ky., as related by Hamburger and Mayers,¹ Fox and Hamburger² and Levy and Alexander.³ At this camp pneumococcus pneumonia appeared early in the autumn of 1917 and continued at the rate of about 50 cases a month throughout the winter. Streptococcus infections began to occur quite early also, and the same was true of measles. It is noteworthy that almost from the start the streptococcus infections showed a great diversity in their local manifestations. In some of the measles cases bronchopneumonia developed, but mortality from this at first was about what would be expected in measles occurring among adults in civil communities. Very soon, however, there became noticeable a marked increase not only in the incidence of streptococcus infections, but also in the severity and types of the cases. While the epidemic in question was by no means confined to the measles cases, and was very properly regarded as separate from the measles epidemic, these patients evidently not only offered the least resistance to the infection but proved a peculiarly favorable soil, so that complications of every conceivable nature became only too common. Of these, bronchopneumonia, with a remarkable tendency to empyema, was the most frequent and the most fatal (47 per cent.—Cole).

Bacteriological investigations revealed the presence of a *hemolytic streptococcus* in the corresponding lesions. In the bronchopneumonia cases this organism was found in the blood, in the sputum and in the lungs, mostly in pure culture, but occasionally associated with a bacillus which Cole⁴ regarded as the influenza bacillus. The relation of the latter to these cases is not clear, but in all likelihood it is of a

secondary nature. The conclusion which was reached by the commission sent out by the Surgeon-General⁴ was that *the hemolytic streptococcus in question was the causative agent of the epidemic.*

In investigating the origin of the epidemic, and particularly the manner of infection in the measles cases, it was ascertained by the Surgeon-General's Commission, at Fort Sam Houston, that of 69 measles cases 39, *i. e.*, 56.5 per cent., harbored a hemolytic streptococcus in the throat.

In view of the fact that certain observers have maintained that the presence of actively hemolytic streptococci is very rare in normal throats,⁵ the question naturally arose whether this was true in the case of the military population at Fort Sam Houston. For purposes of comparison, cultures were therefore taken from the patients in a different ward, and one in which no measles cases were kept. To this end a ward was chosen in which the patients were suspected of having tuberculosis, but no other disease. It was found that although the percentage of patients harboring a hemolytic streptococcus was materially lower than in the measles ward, it was nevertheless fairly high, *i. e.*, 21.4 per cent. In two other wards, containing only patients who were thought to have lobar pneumonia, 57.7 per cent. were found to harbor these organisms.

In order to ascertain whether the patients had acquired the hemolytic streptococcus before entering the wards or whether infection had occurred within, 44 measles patients were examined on admission, then again three to five days later, and again eight to sixteen days after admission. The resulting percentages of positive findings were 11.4, 38.6 and 56.8. These figures speak for themselves and prove conclusively that infection in the majority of cases occurred after admission. The same conclusion was reached in a different manner by Levy and Alexander at Camp Zachary Taylor.³ In two of the measles wards non-infected and infected cases were placed in alternate beds, with the result that at the end of a week 66.6 per cent. of the originally clean cases now harbored the streptococcus in their throats.

In order to ascertain whether the men who came to the

hospital already infected with hemolytic streptococci had acquired these in camp or before, throat swabs were taken from 489 recruits, representing both urban and rural communities, as they stepped from the train. Of these 14.8 per cent. showed the presence of hemolytic organisms—which, however, were not further identified. Corresponding studies which were made of a company of 95 men belonging to an organization to which all new men entering camp were attached during the early period of their training, showed that 83.2 per cent. were infected, and it is noteworthy that of the 388 measles cases that were examined, 346, *i. e.*, 77.1 per cent., were found infected on admission. This is in striking contrast to the figures given by Cole as prevailing at Fort Sam Houston.

The conclusion that may be drawn from these studies is that the great majority of the recruits become infected through a relatively small percentage of supposedly healthy carriers, that of the infected, in turn, a certain number become carriers of this order, while others are rendered ill. In some of the latter the resultant malady is of a minor order, such as pharyngitis, tonsillitis, laryngitis, while in others more serious disturbances develop. Measles cases seem to furnish the most suitable soil for the development of the organism, in a manner quite analogous to the occurrence of puerperal fever and erysipelas on the introduction of pathogenic streptococci into a puerperal or a surgical ward. As the epidemic progresses the virulence of the organism is apparently increased, and at its height the clinical picture of a primary sepsis and serositis develops, frequently without any changes in the lungs, and resulting in an appalling death-rate.

That healthy carriers, or carriers at any rate, who are not regarded as ill, are responsible for these outbreaks can scarcely be doubted, even though we are not in a position as yet to assert that a hemolytic streptococcus found in a throat of an apparently healthy person outside of an epidemic zone is capable of giving rise to disease in others. It is conceivable that the organisms which may be found in the throats of normal persons at times when no epidemic exists are non-

pathogenic, and that they develop pathogenic properties only when they fall upon a special soil. On the other hand, we must remember that in large communities, at any rate, maladies due to streptococci are endemic, and that accordingly the carriers in question may in reality be carriers of organisms that are already pathogenic. Apart from our inability to distinguish between pathogenic and non-pathogenic streptococci occurring in normal throats, there is the factor of the wide distribution of organisms of this order which makes us hesitate to speak of all individuals harboring such as carriers, exactly in the same way as we hesitate to look upon persons harboring the pneumococcus IV as carriers.

However this may be, so much is certain that *some* carriers of *some* hemolytic streptococci are a grave menace to others, and should be viewed in the same light as carriers of other disease-producing organisms.

As I have said before, there are many gaps as yet in our knowledge regarding the relationship of some of the common mouth organisms to disease, but practically speaking the conclusion just formulated may stand.

The experience gathered at Camp Zachary Taylor and at Fort Sam Houston corresponds in practically every detail to the findings obtained at the other army posts, as related by Duncan and Sailer,⁶ Irons and Marine,⁷ Cumming, Spruit and Lynch.⁸ The studies of the latter are of especial interest in so far as they made an attempt to classify the hemolytic streptococci found, in accordance with the type of hemolysis that they produced. Their type I corresponds to the *Streptococcus viridans* hemolysis; types II and III to the alpha and beta types of hemolysis respectively of Smith and Brown.⁹ A corresponding analysis of the findings obtained from the throat swabs of 291 measles patients on entrance to the hospital revealed that 187 showed type I and type II hemolysis, and that of these only 4 developed bronchopneumonia; but during this complication type III hemolytic streptococci in all 4 were isolated. 104 of the total number showed type III hemolysis and of these 34, *i. e.*, 33 per cent., developed bronchopneumonia. The writers state that 70 swab specimens from average throats showed

only 6 per cent. of hemolytic streptococci, which corresponds to the findings of Smillie,¹⁰ obtained in civil life. But they do not indicate from what class of material their results were obtained.

Duration of the Carrier State.—Regarding the duration of the carrier state in convalescents from the camp epidemic under consideration, Levy and Alexander state that with rare exceptions the organisms persisted in the throat throughout the patient's entire stay at the hospital, and that on discharge 71.7 per cent. of all of the patients who had entered the measles wards still harbored the organisms in question, and were no doubt capable of infecting others, and of producing disease when and wherever the soil was favorable. Under the circumstances it can hardly be surprising that Irons and Marine⁷ found 70 per cent. of all the men harboring hemolytic streptococci during the latter part of the period of acute respiratory infections (Camp Custer).

Manner of Infection.—As regards the manner of infection there is, of course, a possibility of direct infection through sputum spray, but to judge from the experience gathered at the various camps there can be no doubt that infection through contaminated dust is probably the usual method. This is evidenced by the findings at Camp Zachary Taylor. The infected and non-infected measles cases were here separated, and the patients placed in cubicles formed by suspended sheets. When not in bed in their cubicles the patients were obliged to constantly wear gauze masks, which were changed every day. All attendants were gowned and likewise masked. But notwithstanding these precautions it was found that on placing non-infected cases in an infected ward and isolating them in cubicles they became infected nevertheless. The only medium through which infection could occur under the circumstances was the air, viz., the suspended dust.

These findings demonstrate in the clearest manner possible not only the mode of infection, but also the amazing readiness with which the streptococcus in question was capable of obtaining a foothold.

Habitat of the Organism.—The habitat of the organisms in the upper respiratory tract is as yet unknown, but we may

well imagine that like other pathogenic organisms which gain access to the human body through the air, they probably lodge in the crypts of the tonsils and other nooks and corners connected with the lymphatic structures of this region.

Mode of Invasion.—As to the manner in which the organisms invade the human body, different possibilities exist. In the measles cases where we usually have a more or less marked pharyngitis, laryngitis or bronchitis, it is quite conceivable that the complicating bronchopneumonia is the result of a descending infection. In the others there is probably always an initial lymphogenic infection, which in turn may lead to a generalized septicemia.

Relation between Camp Epidemic Septicemia and the Ordinary Winter Infections Occurring in Civil Life.—An interesting question which arises in connection with the camp epidemic of the winter of 1917-1918 is whether the type of organism, which evidently was responsible for the outbreak, was also the cause of the coexistent winter infections—of non-pneumococcic nature—which prevailed in civil communities, not only then, but which appear in civil communities practically every winter. We have seen that the epidemic could be traced fairly definitely to healthy recruits coming from urban and rural communities; in other words, the infection was carried into the camps from without and did not primarily originate within the camps. If we accept this view, we must also concede that these same carriers, under favorable conditions, could have infected inhabitants of the communities from which they were drafted. Furthermore, we must concede that for every carrier who left his home there undoubtedly must have been at least one carrier who remained at home. In other words, there is no reason for supposing that the percentage of carriers remaining was materially less than the percentage that left. That the remaining carriers in the course of the winter caused the infection of other individuals, and that some of the carriers fell ill themselves can scarcely be doubted, so that we unquestionably have the right to assume that many of the minor winter infections at any rate were due to the same type of carrier as the serious infections occurring in the camps, even though corresponding bacterio-

logical examinations were not made. Investigations in this direction are, of course, urgently needed to establish beyond question the proposition which I have just formulated, viz., that the camp epidemic in all its phases was in reality nothing else than the common type of winter infection which visits us practically every year, that the difference was practically only one of degree of virulence on the part of the organism, and that this in turn was brought to such a high point, owing to the crowding of the camps and the facilities thus afforded for a most extensive degree of "animal passage," in which the presence of a measles soil no doubt played an important role.

This view is well supported by the fact that epidemics of this order were not confined to any special region, but occurred in practically every district of the United States. The fact that the disease was more prevalent in the Southern Department can no doubt be explained on the basis of local conditions.

Relation of Camp Septicemia to Septic Sore-throat.—It has been suggested that the organism found in the camps is identical with the one that has been encountered in connection with the various epidemics of so-called septic sore-throat which have occurred in the United States within recent years, and which have been traced to infection of the milk supply in every instance. Cumming, Spruit and Lynch⁸ state directly that the hemolytic streptococcus in question is of universal prevalence, and has been isolated by them from cases of septic sore-throat in Massachusetts, on the one hand, and in Michigan on the other. They look upon it as the so-called human type which when transmitted to cows' udders by milkers is very apt to spread through the milk supply and thus give rise to epidemics of greater or less magnitude. While the identity of the organisms encountered under such conditions, with the *Streptococcus hemolyticus* found in camp septicemia, can hardly be regarded as proved, we can say at least that both conditions are due to the activity of a hemolytic streptococcus, and that *carriers do play the same important role in the dissemination of so-called septic sore-throat, be this by infecting the milk supply of a community, or directly or indirectly through the air (sputum spray, dust).*

In the course of his investigation of the Boston outbreak, during which 1400 persons were stricken and of which 1043 were investigated, Winslow¹³ found no evidence of cattle disease and no well-defined cases of sore-throat among the milkers. But as cases of sore-throat were encountered among other employees at the farm, he no doubt correctly concluded that actual infection of the milk supply had occurred through a carrier. To this inference the objection might be raised that no evidence of mastitis was found among the cattle. But as Davis¹⁴ subsequently demonstrated experimentally, an ascending infection of the teat and udder may take place through a slight abrasion of the skin by the contaminated hand in the act of milking, without producing any evidence of so-called caking of the bag. We can accordingly well understand how Winslow may have overlooked the existence of mastitis among the cows, even though the demonstration of the organisms in the milk showed this to have been infected. As the milkers themselves showed no evidence of sore-throat, the inference that one or another of these was a carrier is the only possible conclusion that could be reached.

In his investigation of the Baltimore outbreak, during which 1000 persons were stricken, Stokes¹⁵ traced the infection to a definite herd, but also could not locate the infected cow. There was no history of septic sore-throat among the farmers and employees, but systematic bacteriological studies were not made. I myself had occasion to study a number of cases during this epidemic and found that the organism in question was capsulated—which accords with the results obtained by others, and shows that this particular type of streptococcus at any rate differed from that which has been shown to be responsible for camp septicemia. In the Chicago epidemic of 1913, during which 10,000 cases of septic sore-throat developed, Rosenow¹⁶ obtained the "streptococcus pyogenes" directly from the inflamed udder of a cow, and also from the throat of a milker who was suffering with sore-throat, while septic sore-throat existed among other employees.

The Role of Streptococcus Carriers in the Dissemination of Puerperal Fever and Erysipelas finally has been so well established, by circumstantial evidence, it is true, that even in the

absence of bacteriological proof, no reasonable doubt can remain. The connection may be capable of ultimate bacteriological proof in isolated cases, even under existing conditions, but a final verdict will in many cases only be possible when once our knowledge of streptococcal strains has advanced to a point where such strains can be definitely recognized and their properties foretold in the laboratory. So far as our present knowledge goes we are unable to distinguish between a streptococcus capable of causing erysipelas and one causing puerperal fever, nor can we distinguish such organisms from those found in camp septicemia or in some cases of septic sore throat. Whether any differences exist is indeed a question, and it is not improbable that future studies will show that there is but one type of streptococcus pathogenic for human beings, and that the diversity of lesions is not so much, if at all, due to specific properties on the part of the organism as to differences in the nature of the substances, *i. e.*, the tissues that are attacked.

The Recognition of Streptococcus Carriers.—In view of our imperfect knowledge of streptococcus strains, and above all in view of our inability to foretell, in the laboratory, the virulence and the specific pathogenic properties of organisms belonging to this group, we are obliged to confine our account of the recognition of streptococcus carriers to a consideration of those gross types which have been found in connection with definite pathological anatomical conditions. The term streptococcus after all is a purely morphological term, and presages nothing regarding the biological, let alone the pathogenic, properties of the organism. For some time the streptococcus family was divided into two groups, according to the length of the chains; a *Streptococcus longus* and *brevis* was accordingly spoken of. It goes without saying that such a classification was warrantable as much as would be a division of human beings into such with long legs and others with short legs. In 1903 Schottmüller¹¹ proposed the classification of the streptococci found in connection with lesions occurring in the human being according to the appearance of their colonies upon human blood agar. He thus recognized two groups, *viz.*, one producing hemolysis on this medium—

Streptococcus hemolyticus—while the other formed green, non-hemolyzing colonies—*Streptococcus viridans*. In addition to these a third type was recognized, which is characterized by the constancy with which it forms large capsules, thus resembling the pneumococci. Further studies have shown that most of the organisms of this latter group are bile soluble and ferment inulin, and for this reason, as well as the fact that corresponding organisms have been found in certain cases of lobar pneumonia, this type is now looked upon as a pneumococcus and not a streptococcus, and is termed *pneumococcus mucosus capsulatus*.¹² Occasional strains are, however, at times met with which neither ferment inulin nor are bile soluble and which may possibly represent a separate group to which the term *Streptococcus mucosus capsulatus* should be confined. Of the group as a whole, which evidently stands between the streptococci in the old sense of the term, it is said that its members rarely cause hemolysis, but it should be borne in mind that the organism which has been found in septic sore throat has been described as a hemolytic capsulated streptococcus. From these data in themselves it is clear that this classification also is not satisfactory. The same may be said of that proposed by Smith and Brown,⁹ on the basis of the types of hemolysis which the organisms produce.

More recently Kinsella and Swift¹⁸ have studied large numbers of strains of both hemolytic and non-hemolytic streptococci on the basis of their immunological reactions, and have found that whereas no two of the non-hemolytic strains behaved in an identical manner, the hemolytic variety is homogenous, consisting of members that are nearly identical. This discovery represents real progress in our knowledge of this group of organisms, and constitutes a promising basis upon which future studies may be carried on.

Demonstration of the *Streptococcus Hemolyticus* in Carriers.—Swab cultures are made, on blood agar plates, from the pharynx and tonsils of the individuals to be examined, and incubated for twenty-four hours. Pneumococcus colonies will then appear surrounded by a narrow greenish zone of discoloration, which is due to a slight degree of hemolysis,

associated with methemoglobin formation. This type Smith and Brown refer to as type I hemolysis. *Streptococcus viridans* on the same medium produces green, non-hemolyzing colonies resembling those of the pneumococcus. The *Streptococcus hemolyticus*, on the other hand, produces a very distinct zone of hemolysis, measuring from two to three millimeters in diameter. This type of hemolysis has been subdivided into an alpha and a beta type, which Smith and Brown refer to as types II and III. Type III according to Cumming, Spruit and Lynch represents the *Streptococcus hemolyticus* with which we have been especially concerned in the foregoing pages.

Streptococcus mucosus finally causes hemolysis of the same type as *Streptococcus hemolyticus*. Attention is directed to it on the plate by its growth in large mucoid colonies.

In order to definitely identify the *Streptococcus hemolyticus* hemolyzing colonies are now fished and studied in pure culture in reference to their cultural characteristics, the morphology, the staining reaction, the bile solubility, and fermentative and hemolytic activity of the corresponding organisms.

Their *hemolytic activity* is tested by adding to a given volume of a twenty-four-hour bouillon culture an equal volume of a 5 per cent. emulsion of the red cells of a rabbit or sheep, and noting the degree of hemolysis after incubating for two hours at 37° C.

Bile solubility is tested by adding sterile rabbit or ox bile* to a twenty-four-hour growth in bouillon in the proportion of 0.1 c.c. of the former to 1 or 2 c.c. of the latter, and incubating for half an hour at 37° C. At the end of that time a pneumococcus culture will have cleared, while a streptococcus culture remains turbid. In the absence of bile a sterilized 10 per cent. solution of sodium taurocholate or sodium glycocholate in normal salt solution may also be employed, and used in the proportion of 1 to 5, or 1 to 10 of the cultures.

* This is prepared as follows: The bile is obtained at the slaughter house, autoclaved for twenty minutes at fifteen pounds' pressure, filtered and again autoclaved, after which it is ready for use.

Identification of the Streptococcus Mucosus.—The streptococcus mucosus is identified by its tendency to grow in large mucoid colonies on the blood-agar plate on which it produces zones of hemolysis similar to those of the Streptococcus hemolyticus. The organism is, however, capsulated, the individual cocci being in close apposition and presenting rounded ends. It does not ferment inulin and twenty-four-hour cultures in broth manifest no solubility upon the addition of bile, nor are they agglutinated by antipneumococcus serum—type III—which clumps the corresponding pneumococcus, with which Streptococcus mucosus has been confused in the past.

Preparation of Hiss's Serum Water Media.—The serum water is prepared as described in the section on meningitis and heated for fifteen minutes at 100° C. in an Arnold steam sterilizer and then treated with approximately 1 per cent. of a 5 per cent. aqueous solution of litmus (sufficient to impart a deep transparent blue color) and 1 per cent. of the various sugars, after which the media are sterilized in the Arnold sterilizer—at 100° C.—for twenty minutes on three consecutive days.

To prepare the inulin medium the inulin is dissolved in water, autoclaved at fifteen pounds for fifteen minutes, in order to kill spores, and then added to the requisite amount of serum, after which the mixture is sterilized fractionally as above. The inulin tubes should be observed for at least forty-eight hours before being read. The pneumococci will cause the cleavage of the substance with resultant acid formation, which leads to coagulation of the serum and reddening of the litmus. Streptococci do not produce this result.

Management of Streptococcus Carriers.—*Quarantine.*—From what we have learned regarding the rapidity and the extent to which the carrier state is apt to develop in the course of an epidemic, it is manifest that the control of the carrier by quarantine is practically out of the question, and any attempt in this direction may from the very start be regarded as fruitless. We have seen that in certain depot brigades fully 80 per cent. of the soldiers were infected, and I have pointed out that fully 70 per cent. of the cases admitted

to the hospitals were still carriers when discharged, so that we may assume that it is only a question of time when an entire camp will become infected. We should accordingly be obliged to begin with the process of quarantining *before* the recruits enter the depot brigades. But as 12 per cent. of these arrive at the camp already infected, it is clear that the entire organization would be rendered ineffective if such a number of men were withdrawn at the very outset of their military training. The same, of course, holds true for civil life, the difference being merely a question of a further increase in the difficulty of handling the situation. In a military community the problem could at least be solved in principle, while in civil life even this would be out of the question.

The problem then is what to do. The only alternative proposition evidently is that we attempt to keep away from carriers those who, according to our present knowledge, would be most likely to suffer if by chance they should become infected. This would mean the isolation of the old and the infirm, for example, from individuals who are evidently suffering from a respiratory disturbance associated with sneezing, coughing and hawking, the introduction of the *face mask* not only into the hospital but also into the private home. In military communities no patient should be permitted to enter a ward containing clean surgical cases or into a ward containing clean measles cases without a previous bacteriological examination. No attendants should be permitted in these wards who are carriers, and those whose duty it is to visit both clean and dirty wards should be freshly gowned, capped and masked. The isolation of susceptible individuals should be continued until their health has been sufficiently restored as to render the occurrence of dangerous complications or sequelæ unlikely. In military hospitals the cubicle system should be employed altogether in those wards in which susceptible patients are confined, but the isolation should be carried out more completely than is possible by the sheet method alone.

In civil communities the hospitalization of all measles cases would, of course, be the ideal plan, the patient being

first placed in a detention ward until the necessary bacteriological examination can be made, after which he would be transferred to a clean or dirty ward, as the case may be. In this manner the spread of measles not only would be curtailed, but also the dissemination of hemolytic streptococci whose virulence is increased through measles passage. In the case of the well-to-do, transfer to a hospital, it is true, might not be necessary, but its many advantages in the case of the poor are so obvious as to require no further discussion.

Exclusion of Carriers from Food Supply.—That an individual who is suffering from a streptococcus infection should not be permitted to handle or prepare certain articles of food goes without saying, and it would follow that he should be excluded from such an occupation until bacteriological examination has shown that he is not a carrier. The necessity for such precautions is apparent at once if we bear in mind that practically every one of the serious epidemics of septic sore-throat, so-called, which has occurred in many of our large cities during the past few years has been traced to a definite milk route and could be shown to be more or less intimately connected with an individual harboring the corresponding organisms in his throat. The difficulties which stand in the way of a successful preventive campaign against epidemics of this order are, however, so great that success could hardly be hoped for so long as raw milk is allowed to be sold. It accordingly follows that our simplest and most effective course would consist in securing the universal enactment of a law prohibiting the sale of unpasteurized milk in all large communities.

Septic sore-throat should be made a notifiable disease. Its victims should be bacteriologically controlled during their convalescence and carriers subjected to the same regulations as those which apply to the control of diphtheria and typhoid carriers.

Extension of Carriers from Surgical Wards and Operating Rooms.—The connection between streptococcus carriers and puerperal fever is another problem that requires investigation, as does the relation of carriers to those occasional streptococcus infections which occur even in our best surgical

services. In the olden days of the midwife, and when the rubber glove had not yet been introduced, puerperal fever was only too common, and then rightfully, no doubt, referred to manipulation with infected hands. But even nowadays puerperal fever has not entirely disappeared, even from our best obstetrical services, and there are still deaths from this cause, the origin of which goes unexplained. Some of these cases may represent auto-infections, and occur in individuals who happen to be suffering from some respiratory ailment, apparently of a minor nature, at the time of their confinement. If this be so it would be indicated that cultures be taken from the throats of every such case and that suitable methods be put into operation to prevent auto-infection if the person should prove to harbor dangerous organisms. It would similarly suggest itself that passive carriers among the attendants be either eliminated or gowned, capped and masked when in the room or cubicle of the patient. That similar precautions in every surgical service would not be amiss, especially in winter time, when respiratory ailments with consequent coughing are so common, hardly requires mention.

Prophylactic Vaccination.—In connection with the problem of camp septicemia, and in view of the apparently hopeless task of guarding against the dangers arising from streptococcus carriers by quarantine, prophylactic vaccination has been suggested as worthy of a trial. This seems thoroughly logical not only in view of the fact that in the animal experiment it is possible to produce a considerable degree of resistance against streptococci, but also since it has been shown in the human being that it is manifestly possible to secure resistance against the closely related pneumococcus. (See section on Pneumonia.) In this connection it is interesting to recall that among the 12,519 men who were vaccinated by Cecil and Austin¹⁷ against the three fixed strains of pneumococci (I, II and III) at Camp Upton in the latter part of the winter of 1918, 7 only subsequently developed streptococcus pneumonia (6 of the hemolyticus and 1 of the viridans type), while among the 19,481 unvaccinated men there occurred 106 cases of streptococcus pneumonia (72 of the

hemolyticus and 34 of the viridans type) during the same period of time (ten weeks). Translated into percentages this means that of the vaccinated troops 0.055 per cent. only developed streptococcus pneumonia while the incidence among the non-vaccinated men was nearly ten times as great, viz., 0.54 per cent. It would appear, moreover, that the protection afforded by the pneumococcus vaccine against streptococcus pneumonia was fully three times as great for the viridans as for the hemolyticus.

Especially convincing are the results which were noted among the 3500 colored troops, half of which were vaccinated while the remainder went unvaccinated. Among the former only 2 cases of streptococcus pneumonia developed during the period of subsequent observation, while 28 occurred among the unvaccinated men, although these men were living in the same part of the camp and closely associated on drill grounds and in recreation and amusement halls.

These results, of course, were most surprising, and while the incidence of pneumonia at the time was not nearly so great at Camp Upton as in some of the other camps, and while the absolute figures accordingly are not so striking, there can be no question regarding the facts. This being so, we can only say that if results like these can be obtained with a *pneumococcus* vaccine there should be no delay or hesitancy about the use of a corresponding streptococcus vaccine, which, indeed, might well be combined with the former and used not only in our military camps but also in our civil communities as a preventive against "winter infections." Although the latter are relatively unimportant, aside from the pneumococcus pneumonias, so far as fatalities go, they are very important nevertheless both from an economic standpoint and that of personal comfort. Evidently a great step has been made toward the conquest of this entire group of diseases, and it will be with the greatest interest that we shall look forward to the results that will be obtained in our camps during the coming winter.

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INFLUENZA (PFEIFFER TYPE).

THE bacillus which was first described by Pfeiffer in 1892¹ is now accepted as the causative agent of a certain type of pandemic influenza. All investigators who have been able to study this question at a time when grippe of that type has been prevalent have been able to confirm Pfeiffer's observations and have come to the same conclusion.²

Any doubt that may have existed in the past was largely due to the fact that, *clinically*, we are not able to distinguish between grippe due to the influenza bacillus and grippe due to such organisms as pneumococci, streptococci, various diplococci resembling the meningococcus, etc. It would evidently not be justifiable to conclude that Pfeiffer's bacillus is not the cause of a form of pandemic influenza, on the ground that this organism is not found in clinical grippe at a time when the pandemic form of the malady is on the decline or has already disappeared. Tedesco,³ Ruhemann⁴ and notably Scheller⁵ have shown that whereas maximal percentage findings of Pfeiffer's bacillus will be obtained at a time when this form of pandemic grippe is in full sway, the figures will progressively decline during subsequent secondary outbreaks and in proportion to the extent to which ordinary grippe again comes to the foreground, so that after a number of years the influenza bacillus will be met with only exceptionally while pneumococci and streptococci especially again control the situation. This is well illustrated by Scheller's figures: During the winter of 1906-1907, when influenza of the pandemic type occurred in Germany, Scheller found influenza bacilli in 90 per cent. of the sputa which had been sent in with the diagnosis of influenza. During the winter of 1907-08 this figure dropped to 20 per cent., and during the following summer and the winter of 1908-1909 not a single sputum that was sent in from grippe cases contained the organism in question but pneumococci instead.

Another objection which was raised to Pfeiffer's claim that his organism was the cause of influenza in 1889 to 1892 was the observation that the organism in question could be found not only in individuals who were suffering from the malady at the time, but also in persons afflicted with other diseases, notably phthisis, measles, scarlatina and diphtheria, as well as in people who were to all appearances perfectly well and who had not passed through an attack of influenza. That the true meaning of such findings was not appreciated at the time can scarcely be surprising, while in view of subsequent and similar observations in connection with cholera, typhoid fever, diphtheria, etc., it is of course perfectly clear to us that they do not represent an argument against the pathogenic character of the disease but merely indicate that in *influenza also carriers are of common occurrence*. The frequent presence of the organisms in the sputa of patients suffering from other diseases at the time merely indicates that such maladies create a particularly favorable soil for the development of the influenza bacillus. We have seen before how readily measles cases fall prey to hemolytic streptococci, and in influenza we probably have analogous conditions.

Unfortunately we are as yet in comparative ignorance regarding many of the phases of the carrier problem in connection with influenza, but enough has been learned to warrant the conclusion that *in the dissemination of this malady also, carriers both of the active and the passive type play a very important role*.

Scheller thus noted that during the epidemic of 1906-07, of 109 supposedly healthy individuals, 25 (*i. e.*, about 24 per cent.) harbored the influenza bacillus in the nasopharynx. Of the total number 20 had passed through an attack of the malady, and of these in turn 15, *i. e.*, 75 per cent., gave a positive result; 89 gave no history of a past attack, and of these in turn 10, *i. e.*, 11 per cent., were carriers. These figures are, of course, based on too small a series of examinations as to warrant any far-going conclusions regarding the quantitative role which carriers, as compared with patients, play in the dissemination of the disease.

Duration of Carrier State.—Scheller unfortunately does not mention how long after the attack the individuals were examined nor how long the carrier state lasted, and so far as I have been able to ascertain no other studies in this direction have as yet been made. That the organisms may persist in tuberculous individuals for a particularly long while is suggested not only by Scheller's observation, that at a time when influenza bacilli were no longer found in the sputa of cases that had been diagnosed as grippe, 3 per cent. of the tuberculous sputa still contained the organisms in question, but also by actual observation in concrete cases, where they could be demonstrated years after the attack.

Practically important, from the standpoint of the dissemination of the malady, is the fact that influenza may assume a chronic course, and that in such individuals also the organisms may persist for months and even years. (Pfeiffer, Leichtenstern⁶).

In fine, we must bear in mind that, as in other respiratory infections, some cases run so mild a course as hardly to attract the patient's attention to his own condition, and it goes without saying that such individuals also play an important role in bringing about the spread of the disease.

Origin of Secondary Outbreaks.—The discovery that some individuals may harbor the influenza bacillus for a long time enables us to understand how secondary outbreaks may occur through a period of years when once the disease has appeared in a given locality. The cause for wonder is not so much that such secondary outbreaks do occur, but rather that the malady dies out after a certain length of time. This is usually explained by assuming that suitable soil is no longer available; that an entire community has become immune, in so far as a natural immunity did not exist already before in some. Of the production of such an immunity, however, we have no laboratory evidence, and we may assume as well that through animal passage of a kind the organism has gradually lost its virulence, just as we assume that through animal passage of a kind it may increase or regain its virulence.

Habitat of the Organism.—As regards the habitat of the organism in healthy carriers, Scheller found that positive

cultures are most apt to result if the secretion is obtained from the pharyngeal tonsil. This should be borne in mind, if a bacteriological diagnosis is desired, in clinically doubtful cases.

Mode of Infection.—From the studies of Pfeiffer we know that the viability of the influenza bacillus outside of the human body is relatively slight when perfectly dry, but that in the presence of moisture the organisms retain their power of infecting for at least a fortnight. Pfeiffer concludes from his experiments that the dissemination of the disease through dried sputum by currents of air probably only occurs to a limited degree, and that infection usually takes place through a direct transference of the fresh and moist secretions of the nasal or bronchial mucosa. In other words, we have reason for believing that the dissemination of the disease takes place essentially through sputum spray from patients or carriers.

Concrete examples illustrating the activity of carriers in the dissemination of the disease are not as yet available, and it is scarcely likely that major epidemics will lend themselves to studies of this sort.

The Recognition of Influenza Carriers.—As the influenza bacillus readily dies when kept in the dry state, for even a very short time, it is essential to have the necessary culture media right at hand when individuals are to be examined in order to ascertain whether they are carriers.

The necessary secretion is best obtained by the aid of the West tube, remembering that the pharyngeal tonsil seems to be the favorite habitat of the organism in question. If such a tube is not available one will have to give the wire of an ordinary swab the necessary curve, so as to enable one to pass behind the veil of the palate. The mop itself should, of course, be sterile, and care be taken to avoid contact with the secretions of the mouth itself.

Culture Medium.—For purposes of culture, blood-agar is necessary. While pigeon blood gives particularly good results, human blood or the blood of the usual laboratory animals is perfectly satisfactory. As it is the hemoglobin which the influenza bacillus requires, and as this is needed only in very small amounts, it is not necessary to prepare the blood-agar

in the usual manner by adding a larger volume of blood to a tube of liquefied agar and then plating or slanting the mixture. Perfectly satisfactory results will be obtained if a few loopfuls of a fairly rich corpuscle emulsion are smeared over the surface of an ordinary agar slant a short while before preparing the culture; the amount may be so small that no color is imparted to the agar. Sub-cultures are prepared in the same manner and had best be renewed every four or five days though the organism will usually be found in a viable condition even after a fortnight. The use of plates for initial cultures is, of course, advantageous, but not a necessity.

After smearing the surface of either plates or slants the cultures are kept at 37° to 40° C. for from eighteen to twenty-four hours, when they are examined.

The influenza bacillus grows in the form of minute, transparent, drop-like colonies which manifest no tendency to coalesce, but remain perfectly discrete and are usually quite numerous.

Such cultures form a marked contrast to control cultures on plain agar on which no growth of the influenza bacillus at all takes place, and only isolated colonies of organisms, such as streptococci, pneumococci and the like appear.

In the beginning, before the observer has gained the necessary experience, it is advisable always to prepare such control cultures for comparison with those obtained on the blood-agar.

In the New York Board of Health laboratories the following medium has been employed during the recent epidemic of influenza: Plates are charged, each with 12 c.c. of neutral 5 per cent. glycerin-veal infusion agar, to which 0.5 c.c. of sterile citrated horse blood is then added at a temperature of from 90° to 100° C. The blood and medium are carefully mixed, so as to produce no bubbles, when the plates are allowed to cool and tested for twenty-four hours for sterility. The blood used is citrated by mixing 1 part of a 10 per cent. solution of sodium citrate in saline with 10 parts of blood under sterile precautions. On this medium the influenza bacillus grows readily and quite profusely.

Microscopic Appearance of the Influenza Bacillus.—For microscopic examination it is well to stain one smear accord-

ing to Gram—counterstaining with saffranin—to which the organism is negative, and another with dilute carbol-fuchsin, Fränkel's carbol-gentian-violet or Sterling's gentian violet—exposure for about five minutes.

Aside from its negative behavior to Gram the pleomorphism of the influenza bacillus is particularly characteristic. While the organism is usually described as a bacillus, measuring about $0.5\ \mu$ in length by 0.2 or $0.3\ \mu$ in breadth, the beginner is very apt to mistake it for a coccus, and more particularly for a diplococcus, as it shows a marked tendency to grow in pairs, arranged end to end.

Involution forms are also seen quite frequently, among which giant forms with club-shaped ends—usually single—are common. Various writers further have described the occurrence of so-called pseudothreads in cultures of the organism. Such formations Pfeiffer was originally inclined to regard as pseudo-influenza bacilli, but he convinced himself that thread formation could unquestionably occur in pure cultures of the influenza bacillus proper. They are now viewed as involution forms.

In stained specimens it will be noted that many of the organisms stain more deeply at the ends than in the middle; this is shown particularly well in the Gram specimens after counterstaining with safranin.

The identification of the influenza bacillus by serological methods is not practical, owing to the difficulties attending the immunization of animals. Very few investigators have been able to obtain agglutinating sera with a titer of 300 or more, and then only at the expense of a very large number of animals.

For the present, then, the recognition of the influenza bacillus will have to be based upon its absolute hemoglobophilia, its pleomorphism, the tendency to polar staining and its negative behavior to Gram.

Management of the Influenza Carrier.—The same remarks apply here that have been made in connection with the consideration of streptococcus carriers. Our prime consideration should, of course, be to attempt to prevent the production of carriers rather than the quarantine of the latter. To

this end every effort should be made to prevent the disease from gaining headway when once it has appeared. This may be attempted, on the one hand, through a *most widespread and continuous instruction* not only of the public, but of the general practitioner as well, who himself is but rarely sufficiently trained in sanitary work to undertake such a problem on his own initiative and, on the other, in the isolation of every case of recognized influenza. In connection with our present epidemic the public and the medical profession, both in civil and military life, were found completely unprepared, and, as a consequence, no steps that were taken when the disease had once obtained a proper start were found to avail. To the thoughtful observer it has been a shock to find influenza patients placed promiscuously in the general wards of our hospitals, and that no attempt at masking had been made for a long time which latter, of all prophylactic measures in connection with the dissemination of respiratory infections is, after all, the one single method that is of unquestionable value.

Whether or not vaccination against influenza will prove successful time only can tell, but on theoretical grounds it would certainly appear to be indicated. In any event it would appear wise to vaccinate against the complicating pneumococcus and streptococcus pneumonia, using a vaccine such as that which has been described under the corresponding headings.

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APPENDIX.

THE unfortunate lack of recognition on the part of the State and municipal health authorities of our country of the importance of carriers in the dissemination of infectious diseases is best illustrated by the complete absence of any specific laws or regulations appertaining to their management, up to the year 1915, and by the small number of States and municipalities which have enacted such laws since that time. This is a serious reflection both upon the intelligence and the statesmanship of our law-making bodies as well as upon the efficiency of those medical officers who have been entrusted with the duty of safeguarding the public health.

The few regulations which have actually been enacted up to January 1, 1918, are given below and have been arranged in two series, the first comprising the State laws and regulations relating to carriers, and the second the corresponding municipal ordinances and rules as based upon the public health records issued by the United States Public Health Service. An analysis of these laws will show at once that some steps have been taken in the right direction, but that for the most part the laws do not go far enough, that in themselves, without supporting legislature, they will not lead to the desired end for the reason that provision has only exceptionally been made for an elevation of the corresponding boards of health to that state of political and financial independence in the absence of which modern sanitary work cannot be properly carried on.

STATE LAWS AND REGULATIONS PERTAINING TO INFECTION CARRIERS.

ARIZONA.

No specific regulations.

CALIFORNIA.

(Reg. Board of Health, August 1, 1914, and September 4, 1915.)

RULE 8.—*Diphtheria*.—When isolation and quarantine for diphtheria have been established in accordance with Rules 6 and 7, any person living within the quarantined premises, but staying at all times outside the area of isolation, may be given permission by the local health authority to go to and from the premises if the following conditions have been met: Cultures taken from his nose and throat and submitted to a State or municipal laboratory must have been reported as negative for diphtheria. All other members of his household must, if possible, have had cultures taken from their noses and throats, and those persons whose cultures were found positive must be isolated so that there is no contact with him. He must also agree to avoid any occupation or practice which would make him especially dangerous in the event of his becoming a carrier. The local health authority may revoke this permission if the above provisions are not complied with.

In his investigation of a case of diphtheria the local health authority shall make inquiry regarding those who have come in contact with the patient, and if any of them contemplate leaving the jurisdiction of the local health authority within two weeks after the last exposure the local health authority shall notify the State Board of Health of their names and destinations.

NOTE 1.—Rule 8 permits the wage-earner to continue his occupation unless he has already become a carrier or unless his occupation is such that he would probably infect others if he became a carrier. Such occupations are such as the production or handling of milk and any work which involves contact with large numbers of persons, especially young children.

NOTE 4.—The purpose of the establishment of an area of enforced isolation within the quarantined premises is not only to prevent acute cases among the contacts, but especially to diminish the formation of carriers. Under the previous

system of enforced quarantine with optional isolation the formation of carriers frequently occurred. Carriers are much more dangerous to the community, in the aggregate, than the acute cases.

NOTE 5.—Although diphtheria antitoxin is efficient in preventing contacts from contracting diphtheria, it will not prevent their becoming carriers. Therefore no relaxations of the precautions against contact with infectious persons can be permitted to those who have been immunized. Persons immune owing to previous attacks of the disease also may become carriers and must observe the precautions.

RULE 9.—*Release from Quarantine.*—As soon as a diphtheria patient is free from all symptoms, the attending physician shall notify the local health authority of the fact. The local health authority or his representative shall thereupon make an investigation, and, if he finds that the case has made a complete clinical recovery, as reported, he shall take cultures from the nose and throat of the convalescent at intervals of not more than a week and not less than forty-eight hours, and shall submit them to a State or municipal laboratory. Where it is impractical for a local health authority or his deputy to take the cultures, he may permit the attending physician to represent him for that purpose. As soon as two successive negative cultures from both nose and throat have been obtained the local health authority shall terminate the quarantine and the isolation. If two successive negative cultures cannot be obtained from the convalescent within one month after recovery he is to be regarded as a carrier and the quarantine is to be terminated, leaving the isolation in force until removed according to Rule 10. If the area of isolation and the quarantined premises coincide the warning card for isolation is to be substituted for the placard for quarantine.

RULE 10.—*Release from Isolation.*—At the end of four weeks after complete recovery from diphtheria, as determined by the local health authority in accordance with the provisions of Rule 9, if positive cultures are still obtained, the local health authority shall at once report to the State Board of Health the circumstances of the case and shall

recommend either a continuation of isolation or release from isolation under certain specified restrictions. Isolation is not to be continued for more than six weeks after complete recovery, except when specified by the State Board of Health. When isolation is terminated the objects in the area of isolation must be disinfected.

RULE 11.—*Diphtheria Carriers*.—Any person who has been free from symptoms of diphtheria for a month or longer and who harbors diphtheria bacilli is a carrier. Any known or suspected diphtheria carrier shall be reported to the local health authority, who shall investigate and report to the State Board of Health. Pending the receipt of instructions from the State Board of Health the local health authority shall isolate or quarantine the carrier if in his judgment the danger to the community necessitates such action. In the event of any known or suspected carrier leaving the jurisdiction of a local health authority the State Board of Health shall be notified by the local health authority of the name of the carrier and his destination.

RULE 12.—*Epidemiological Investigation*.—Whenever a local health authority receives reports of the existence of diphtheria within his jurisdiction or is notified by the State Board of Health that cases of diphtheria reported from other communities have probably received the infection within his jurisdiction, he shall conduct an investigation to ascertain the sources of infection and shall report the results to the State Board of Health. He shall immediately take such action for the protection of the community as may be indicated by the conditions discovered or suspected in the course of his investigation.

NOTE 1.—*Diphtheria in Schools and Institutions*.—If diphtheria appears in a school or public institution, and there is reason to suspect that the disease was contracted within the institution, cultures from the noses and throats of all the officers, teachers, pupils and inmates of the institution shall be taken, in order that the epidemic may be promptly checked by isolation or exclusion of the carriers.

When diphtheria is present in a community, teachers must send home any children who come to school showing symp-

toms suggestive of infectious disease and must report at once to the local health authority, so that he can make an investigation and determine whether it is safe for the child to return to school. During an outbreak of diphtheria teachers shall also report to the health authority the return to school of any pupil after an unknown illness, so that it may be determined whether he is a diphtheria carrier.

COLORADO.

No specific regulations.

DISTRICT OF COLUMBIA.

There are no regulations covering infection carriers as such. Carriers of infection are regarded as active clinical cases from the point of view of regulating the control of a given disease.*

CONNECTICUT.

(Sanitary Code, Chapter I, Communicable Diseases, 1918.)

Definition of the Term "Carrier."—A carrier is one who harbors in his body the microörganisms of a communicable disease, but who at the time is apparently in good health. A carrier may convey the infectious agent to another person and, under favorable conditions, the germs may incite the disease in his own body.

REGULATION 22.—*Presumably Exposed Persons May be Examined and Controlled.*—When a health officer has reasonable grounds to believe that a person or persons may have been exposed to a communicable disease, he may control them as known contacts, making such examinations and adopting such measures as he deems necessary and proper for the protection of public health and the prevention of the spreading of disease.

REGULATION 23.—*Methods of Isolation of Carriers.*—Carriers of the infectious agent of asiatic cholera, dysentery, bacillary, paratyphoid, typhoid fever, shall be controlled

* As per Letter from the Chief of the Bureau of Preventable Diseases.

by isolation or restriction of movement until repeated examinations of excreta show the absence of the infectious agent.

NOTE 2.—It is desirable when possible to release cases of dysentery, amebic, dysentery, bacillary, typhoid fever only after the disappearance of the infective organisms has been shown by laboratory examinations of the excreta.

REGULATION 24.—*Removal to Hospital of Certain Cases.*—When in the opinion of the health officer or the State Commissioner of Health proper isolation or quarantine of an affected person or persons, carrier or contact is not, or cannot be, effectively maintained on the premises occupied by such person or persons by methods designated in this chapter, he may remove or require the removal of such person or persons to a hospital or other proper place designated by him; or he may employ such guards or officers as may be necessary to maintain effective isolation or quarantine.

REGULATION 32.—*Observance of Quarantine and Instructions.*—Every person who is affected with a communicable disease, who is a carrier of the germs of a communicable disease, or who is suspected of having come in contact, directly or indirectly, with a case of communicable disease, shall strictly observe and comply with all orders, quarantine regulations and restrictions given or imposed by the local health authority or the State Commissioner of Health in conformity with law.

Carriers of the infectious agent of diphtheria shall be isolated until two successive cultures from both the nose and throat, taken at least twenty-four hours apart, show the absence of the Klebs-Löffler bacillus.

NOTE 1.—In cases in which the organism persists for an unduly long time after convalescence, cultures should be submitted for a virulence test to a laboratory approved by the State Department of Health or the advice of the State Department should be sought.

Carriers of the infectious agent of cerebrospinal meningitis shall be isolated until examination of the nasal and throat discharges show the absence of the specific diplococcus.

IDAHO.

(Reg. State Board of Health, May 13, 1914.) Quarantiné.

RULE 18.—*Diphtheria*.—For the patient: Isolation for fourteen days after recovery of cases of diphtheria may be released from quarantine when two cultures from the throat examined by the State Board of Health laboratory three days apart show the patient to be free of the disease.

For exposed persons: Quarantine for fourteen days from last exposure or until two successive cultures from the throat made three days apart show the absence of diphtheria bacilli.

ILLINOIS.

(Reg. Board of Health, February 16, 1915.)

RULE 1.—Every physician, attendant, parent, householder or other person having knowledge of a known or suspected case of typhoid fever, or of a person known or suspected to be a "*typhoid carrier*," must immediately report the same to the local health authorities.

RULE 12.—Any person known to be or suspected of being a typhoid "carrier," and therefore capable of spreading typhoid infection, shall be treated as a typhoid patient even though to all outward appearances such person may appear to be well, and shall be subject to the rules governing typhoid fever cases: Provided, however, That in order to meet conditions peculiar to individual cases the State Board of Health, upon its own initiative or upon recommendation of the local health authorities, may modify or relax these rules.

RULE 7.—A person recovered from typhoid fever will not be permitted to engage in any manner in the handling or preparation of foodstuffs, milk or milk products, including the handling of milk containers, until one month after date of recovery, and until after the intestinal discharges have ceased to be more copious, liquid or frequent than normal, or until such time as it has been ascertained that such person is in no danger of spreading the infection.

Typhoid Fever.—Rule 5 (c).—*Convalescents*.—No person recovered from typhoid fever shall be permitted to engage

in any manner in the handling or preparation of foodstuffs, milk products, including the handling of milk containers, until the stool and urine of such persons are found by laboratory examination to be negative to typhoid bacilli.

NOTE.—Examinations of stool and urine for typhoid bacilli will be made free of charge at the laboratory of the State Department of Public Health, Springfield. Containers for forwarding specimens will be furnished on request addressed to the laboratory of the Department at Springfield.

Penalty for Violation.—A fine of not more than \$200 for each offence or imprisonment in the county jail not exceeding six months, or both.

Epidemic Meningitis.—Rule 3.—Quarantine.—Occupants of the premises on which the case exists or others who have been exposed to the case should be confined until cultures have been made and it has been determined by laboratory examination that they are not “carriers” of the disease.

Occupants of the premises *proved not to be carriers* and who desire to leave the quarantined premises may be removed after disinfection of persons and clothing, but they must not return to the quarantined premises during the period of quarantine.

If any such removed occupants are school children or school teachers they should again be cultured after removal and should not be permitted to return to school until proved by laboratory examination not to be carriers of the disease.

Quarantine of the infected premises should not be raised until the patient or patients have recovered and until two successive negative cultures at three-day intervals have been obtained from the patient and also one negative culture from attendant and all other inmates of the premises and contents have been thoroughly disinfected in manner approved by the State Department of Public Health. (Quarantine in epidemic meningitis cannot be terminated with safety without resort to laboratory examination of cultures.)

INDIANA.

No specific regulations.

IOWA.

(Reg. Board of Health, September 28, 1916.)

RULE 2.—Section 1.—*Diphtheria, Period of Quarantine.*—The period of quarantine for diphtheria shall be determined by release cultures and the following rules shall be rigidly observed:

RULE 1.—*Cultures for Release.*—Cultures for release shall be taken by the attending physician from both nose and throat of the patient, such cultures to be taken not less than two hours following the application of an antiseptic solution to the nose or throat when such treatment has been given.

RULE 2.—*First Culture Taken.*—No cultures for release shall be taken until five days after the disappearance of all membrane or inflammation of the nose or throat.

RULE 3.—*Second Culture Taken.*—Second and subsequent cultures shall not be taken within twenty-four hours of the preceding culture.

RULE 4.—*Cultures for Release Examined by Bacteriologist.*—All examinations of cultures for release shall be made by a bacteriologist appointed by the director of the State Bacteriological Laboratory.

RULE 5.—*Two Negative Culture Reports Necessary.*—Quarantine shall not be released until two consecutive negative reports on cultures have been reported to the attending physician by the bacteriologist.

Diphtheria Carrier after Twenty-eight Days in Quarantine.—In case a person has been in quarantine for twenty-eight days after the beginning of the disease, and still harbors diphtheria bacilli in the nose or throat, as shown by a positive report from the bacteriological laboratory, and in case such person has entirely recovered from the disease, such person shall be regarded as a “diphtheria carrier” and treated as described in Section 4 of this rule.

RULE 6.—SECTION 4.—*Diphtheria Carriers.*—Every person who is a “diphtheria carrier,” that is, harbors diphtheria bacilli in the nose or throat, as shown by a positive report from the bacteriological laboratory, shall be confined to certain premises which shall be placarded “Diphtheria car-

rier here," until such time as the diphtheria bacilli are no longer present or have been found not to be capable of producing the disease, as shown by a report from the bacteriological laboratory. Persons on the premises who are not diphtheria carriers need not be confined to the premises, but may be permitted to go back and forth from the premises to other places, provided cultures have been taken from the nose and throat and sent to the bacteriological laboratory within a day after the premises are placarded and reported to be negative.

Persons on Premises of Carriers.—Persons on the premises from whom no cultures are taken shall be confined to the premises as if they were carriers.

Carriers When Released.—Carriers shall not be released until two consecutive negative reports have been received from the bacteriological laboratory on cultures taken from both nose and throat.

SECTION 5.—*Healthy Persons; How Released from Diphtheria Quarantine.*—Healthy persons living on premises where there is a case of diphtheria may be permitted to leave the premises, provided it has been shown by a report from the bacteriological laboratory on a culture taken from the nose and throat that such persons are not carriers of diphtheria bacilli.

KANSAS.

(Reg. Board of Health, March 20, 1916.)

RULE 10.—Any person who is known to harbor the bacilli, virus or infective agent of any communicable disease, even though manifesting no symptoms of such disease, is hereby declared to be a *carrier* and a menace to the public health, and the name and address of such person shall be reported immediately to the local city or county health officer in whose jurisdiction such person resides. The local health officer shall immediately investigate and report to the State Board of Health. Pending the receipt of instructions from the State Board of Health the local health officer shall isolate or quarantine the carrier, if in his judgment the danger to the community necessitates such action. In the event of

any known or suspected carrier leaving the jurisdiction of the local health authority the State Board of Health shall be notified by the local health officer of the name of the carrier and his destination.

LOUISIANA.

There are no specific legislative enactments relating to infection carriers. The Sanitary Code merely requires that "no cook, assistant cook, waiter or other worker in the kitchen or dining room must be employed by any hotel, restaurant, boarding house or other public eating house . . . who is recently convalescent from pneumonia, diphtheria or typhoid fever."*

MAINE.

There are no specific legislative enactments relating to infection carriers. Reliance is placed on Rule 7 of the Rules and Regulations of the State Department of Health relating to infectious diseases and to Sections 22, 24 and 65 of the Health Laws of the State, which read as follows:

Rules and Regulations Relating to infectious Diseases, 1916.
Rule 7.

Contacts and Suspects.—Persons who have been exposed to an infectious or contagious disease, or who are suspected of having an infectious or contagious disease, *or of being infectious or the carriers of infection*, may be placed under quarantine or observation as is provided in Rule 6, until the period of incubation has elapsed, or until the nature of the disease has been determined, or the period of infectiousness and danger to the public has ended; and said persons shall obey all orders and shall be guided by the instructions which may be given by the local board of health.

Abstracts of Public Health Laws, Chapter 197, Laws of 1917.

SECTION 22.—*Regulations Against Infectious Diseases.*—And the said Board of Health may from time to time, make,

* As per letter from the President of the State Board of Health.

alter, modify or revoke rules and regulations for guarding against the introduction of any infectious or contagious diseases into the State. And the said Board of Health may declare any and all of its rules and its regulations made in accordance with the provisions of this section to be in force within the whole State, or within any specified part thereof, and to apply to any person or persons, family, camp, building, vessel, railroad car or public vehicle of any kind.

SECTION 24.—*Penalty for Refusing to Obey Regulations.*—Any person who shall neglect or refuse to obey the said rules and regulations or who shall wilfully obstruct or hinder the execution thereof, shall be punished by a fine of not more than \$500, or by imprisonment in the county jail for a period of not more than six months or by both fine and imprisonment.

SECTION 65.—*Infected Houses Shall Not Be Let.*—No person shall let or hire any house or room in a house in which any of the diseases have existed for which disinfection may be required by the State Board of Health without having caused the house and the premises used in connection therewith to be disinfected to the satisfaction of the local board of health.

MARYLAND.

“Carriers of communicable diseases are controlled by the powers that are given the State Department of Health to do whatever is necessary to prevent disease being communicated to the well citizens of the State. Therefore in cases of milk outbreaks of typhoid fever examination is made for typhoid carriers and if such persons are found they are excluded from the dairy and confined as much as is deemed necessary to the health officers to protect other people.

“The same is true of carriers of diphtheria organisms until the examinations are found by animal experiment to be non-virulent.”*

* As per letter from the Chief of the Bureau of Communicable Diseases.

MASSACHUSETTS.

No Specific State Regulations Regarding Infection Carriers.—Local boards of health have a right to make and enforce their own regulations without reference to State authority.*

MICHIGAN.

Infection carriers are treated in this State in the same manner as communicable diseases and their control placed under the supervision of the health officer of the community.†

MINNESOTA.

(Reg. Board of Health, November 19, 1913.)

704.—In all cases diagnosed diphtheria, laryngeal croup or membranous croup upon clinical findings or diphtheria upon laboratory findings, two successive negatives on separate nose and throat cultures are required before release of quarantine in cities and villages and in country districts within two miles of a city or village. Cultures should be sent at least once a week after the patient recovers, but no case may be held in quarantine more than six weeks after all clinical symptoms have disappeared.

705.—All members of a household in which diphtheria exists shall be quarantined unless the patient is entirely isolated in a portion of the house used for no other purposes and is in charge of a reliable attendant.

If proper isolation obtains and the laboratory diagnosis on nose and throat cultures from members of the household employed at gainful occupations is "No diphtheria bacilli found," such persons may be released from quarantine, provided they make a declaration in writing to the health officer that they will not come in contact with the patient, the patient's room or any thing or any person coming in contact with the patient or the patient's room. The health officer

* As per letter from the Director of the Division of Communicable Diseases.

† As per letter from the Assistant Secretary.

shall issue written permits of release, which may be revoked if the above provisions are not complied with.

706.—In all cases diagnosed diphtheria, laryngeal croup or membranous croup upon clinical findings or diphtheria upon laboratory findings, quarantine may be released in country districts more than two miles from a city or village three weeks after all clinical symptoms have disappeared, or earlier if two successive negatives on separate nose and throat cultures have been reported in accordance with regulation 710.

707.—Patients released from quarantine upon the expiration of the prescribed quarantine period, whether in cities, villages or country districts, shall not be permitted to attend any public, private, parochial, church or Sunday school, or any public or private gathering, until two successive negatives have been reported in accordance with regulation 710. In such cases the patients may go to their physician or health officer to have cultures taken.

708.—Persons associated with a case and wishing to leave the premises before quarantine is raised shall be separated from the patient and shall have nose and throat cultures taken by the health officer or attending physician. If the laboratory diagnosis is "No diphtheria found," the clothing to be worn or taken away from the house shall be disinfected and the person shall take a full bath before being released.

After fatal cases the members of the household shall not be released from quarantine until the above measures have been carried out.

709.—The control of diphtheria in public institutions shall be governed entirely by laboratory examinations. Immediately after the appearance of diphtheria in an institution the head of the institution shall notify the State Board of Health of the fact. Each person whose cultures show diphtheria bacilli shall be quarantined, whether symptoms exist or not, until one negative report on separate nose and throat cultures has been made, after which the person shall be properly cleansed, the clothing properly disinfected and the party removed from quarantine to detention quarters and kept there until two more successive negative reports

on separate nose and throat cultures have been made, whereupon release may be permitted after proper disinfection.

710.—All cultures must be taken by a physician or sanitary inspector and cultures for release of quarantine shall be taken with at least twenty-four hours intervening. All cultures must be submitted to the laboratory division of the State Board of Health or to a laboratory having the official endorsement of said board. Reports on cultures examined elsewhere will not be officially recognized.

State Health Laws and Regulations, July 16, 1917, p. 43.

Carriers.—Any person proved to be a carrier of disease germs shall be subject to the regulations of the State Board of Health relating to the control of persons who may be infected with said disease.

MISSISSIPPI.

Rules and Regulations of the Mississippi State Board of Health Governing Infectious Diseases, Bulletin, January-March, 1918.

Diphtheria.—(d) Any child attending school that becomes a carrier of diphtheria germs shall be excluded from school and quarantined until proper treatment is given for rendering the throat free of diphtheria bacilli. Said child shall be released from quarantine upon obtaining two negative cultures from the throat and nose taken forty-eight hours apart, provided that during the forty-eight-hour period no spray or gargle is used in the throat and nose.

(e) Any person that becomes a carrier of diphtheria germs shall be isolated and the throat shall be properly treated for the removal of the diphtheria bacilli. The period of isolation for adults or those not attending school shall be left to the discretion of the health officer, but the treatment of said carrier must be kept up until two negative cultures are obtained from the throat and nose taken twenty-four hours apart, provided that during this period no spray or gargle is used in the throat and nose by said individuals.

MISSOURI.

No specific regulations regarding infection carriers.

NEBRASKA.

Rules and Regulations, July 12, 1918, p. 31.

Carriers of Communicable Disease.—It shall be the duty of every county or city or village board of health when they know or have any good reason to believe that any person, although not himself afflicted with a communicable disease, is a carrier of such disease, so as to be a menace to the health of the public, if allowed to go at large, to cause such person to be quarantined in the way and manner set forth under the section "Quarantine;" Provided that the State Health Officer may, when in his opinion it is necessary to do so, place any such person under quarantine. In all cases of quarantine where the party himself is not afflicted with the disease, but is a carrier of same, the quarantine shall continue until such time as it is determined by the proper tests by the State Department of Health that the party is no longer a carrier of contagion or a menace to the health of the public, or until the officer placing him in quarantine removes the quarantine therefrom.

Any person who being placed under quarantine fails, neglects or refuses to comply with the provision of the quarantine, or any person who in defiance of the terms of such quarantine shall go into the place where the person so quarantined is being held, shall be deemed guilty of a misdemeanor, and, upon conviction, shall be fined not less than fifteen dollars (\$15) nor more than one hundred dollars (\$100).

NEW HAMPSHIRE.

No specific regulations regarding infection carriers, 1912.

NEW YORK.

Rules and Regulations.—(Chapter 559, Act of May 17, 1913.)

Control of Dangerous and Careless Patients.

SECTION 326a.—Whenever a complaint shall be made by a physician to a health officer that any person is a carrier of typhoid fever and is unable or unwilling to conduct himself and to live in such a manner as not to expose members of his family or household or other persons with whom he may be associated to danger of infection, the health officer shall forthwith investigate the circumstances alleged. If he should find that any such person is a menace to others, he should lodge a complaint against such a person with a magistrate and on such complaint the said person shall be brought before such magistrate. The magistrate after due notice and a hearing, if satisfied that the complaint of the health officer is well founded and that the person is a source of danger to others, may commit him to . . . a hospital or institution, established for the care of persons suffering from any such disease or maintaining a room, ward or wards for such persons. Such persons shall be deemed to be committed until discharged in the manner authorized in this section. . . .

The chief medical officer of the hospital or other institution to which any such person has been committed, upon signing and placing among the permanent records of such hospital or institution a statement to the effect that such person has obeyed the rules and regulations of such hospital or institution for a period of not less than sixty days, and that in his judgment such person may be discharged without danger to the health or life of others, or for any other reason stated in full which he may deem adequate and sufficient, may discharge the person so committed. He shall report each such discharge, together with a full statement of the reasons therefor, at once to the health officer of the city, village or town from which the patient came and at the next meeting of the board of managers or other controlling authority of such hospital or institution. Every person committed

under the provisions of this section shall observe all the rules and regulations of such hospital or institution. Any patient so committed who neglects or refuses to obey the rules or regulations of the institution may by direction of the chief medical officer of the institution be placed apart from the other patients and restrained from leaving the institution. Any such patient who wilfully violates the rules and regulations of the institution or repeatedly conducts himself in a disorderly manner may be taken before a magistrate by the order of the chief medical officer of the institution. The chief medical officer may enter a complaint against such person for disorderly conduct, and the magistrate, after a hearing and upon due evidence of such disorderly conduct, may commit such person for a period not to exceed six months to any institution to which persons convicted of disorderly conduct or vagrancy or of being tramps may be committed; and such institution shall keep such person separate and apart from the other inmates, provided that nothing in this section shall be construed to prohibit any person committed to any institution under its provisions from appealing to any court having jurisdiction for a review of the evidence on which commitment was made.

Communicable Diseases (Reg. Public Health Council, April 7, 1914).

CHAPTER 2.—*Regulation 40.—Carriers of Disease Germs.*—Any person who is a carrier of the disease germs of diphtheria or typhoid fever shall be subject to the special rules and regulations of the State Department of Health.

Typhoid Fever.—Care of Carriers (Chapter 371, Act of May 1, 1916).

SECTION 1.—Chapter 49 of the laws of 1909, entitled "An act in relation to the public health, constituting Chapter 45 of the consolidated laws," is hereby amended by adding a new section to be known as section 36a, and to read as follows:

SECTION 36a.—*Providing for the Care and Maintenance of Carriers of Disease.*—Whenever an individual is declared by

the State commissioner of health as being a carrier of typhoid bacilli and whenever, for the protection of the public health, the State commissioner of health shall have certified to the necessity of continued quarantine, or whenever in accordance with the rules and regulations adopted by the State commissioner of health a carrier of the germs of typhoid fever is prevented from carrying on any occupation which would enable him to gain a livelihood, such individual may be given hospital or institutional care under the surveillance of the local health officer at the expense of the State, if such hospital or institution in the judgment of the State commissioner of health be properly equipped for the care and maintenance of said individual.

When no such hospital or institution is available, and when in the opinion of the State commissioner of health such individual may be cared for at home or in a private family with due regard to the protection of the public health, the local charities commissioner or overseer of the poor shall, in accordance with the rules and regulations adopted by the commissioner of health, furnish necessary medical attendance and maintenance. No expenditure for the purposes herein authorized shall be contracted for or incurred by any local overseer of the poor or charities commissioner until after such expenditure has been authorized and approved by the State commissioner of health. A verified statement of any such approved expense incurred hereunder shall be transmitted by the local overseer of the poor or charities commissioner to the State commissioner of health. The commissioner of health shall examine this statement, and if satisfied that such authorized expenses are correct and necessary in accordance with the rules and regulations adopted by him he shall audit and allow the same and when so audited the amount thereof shall be paid by the State Treasurer on the warrant of the comptroller to such institution or local poor officer.

Rules and Regulations for Control of Typhoid Carriers.

RULE 1.—A typhoid carrier is a person who harbors typhoid bacilli and emits them, regularly or intermittently. This condition may or may not follow a recognized attack

of typhoid fever. A person continuing to discharge typhoid bacilli following an attack of typhoid fever shall be regarded as a case, rather than a carrier for a period of at least twelve weeks following subsidence of clinical symptoms. After that period, the Health Officer may, in his discretion, declare such a person to be a carrier.

RULE 2.—The Health Officer, upon the discovery of a typhoid carrier, shall immediately report the fact to the State Department of Health, giving the full name, age, occupation, and address of such carrier (together with any other information relative to possible or probable infection of others) and shall also communicate the fact to the carrier himself or his guardian, imparting to him detailed information regarding the precautions to be observed in disposing of his discharges, in preventing contamination of his hands, and thus protecting others from infection. Instruction given by the Health Officer should include a copy of these rules and regulations and directions to wash the hands thoroughly with soap and water immediately after using the toilet and to use individual towels and drinking and eating utensils, which should be thoroughly cleansed, preferably by boiling, before being used by others.

RULE 3.—When an outside toilet is being used regularly by a typhoid carrier, it shall be equipped with a watertight container so screened as to exclude flies, and the removal of the contents for disposal should be in accordance with instructions given by the Health Officer.

RULE 4.—No typhoid carrier may engage in any occupation involving the handling of milk or other food product to be consumed by others. Should a typhoid carrier be discovered upon a dairy farm, the Health Officer may prohibit the sale of milk, cream or butter, except under conditions stated in regulation 37, Chapter II, of the Sanitary Code.

RULE 5. No typhoid carrier shall permanently leave the community in which he resides without notification to the Health Officer, who is to be informed of his destination, including his new address. The Health Officer should immediately notify the State Department of Health of the change of address.

RULE 6. The local Health Officer shall visit each typhoid carrier within his jurisdiction at least once monthly in order to determine whether instructions are being complied with; and once in each quarter shall render a report regarding each such carrier to the State Department of Health upon a form prescribed for the purpose.

RULE 7. The Health Officer shall cause samples of the discharges from each carrier to be examined bacteriologically at intervals at a laboratory approved by the State Department of Health, and a carrier may be regarded as recovered and be discharged from observation when four successive samples, taken not less than seven days apart, shall have been found not to contain typhoid bacilli; except that no negative report shall be considered if the specimen has been delayed in transit, and in no instance if more than two days have elapsed between the collection of the specimen and its examination.

Rules and Regulations for Control of Diphtheria Carriers.

RULE 1. A diphtheria carrier is a person who harbors in the secretions of his nose or throat the bacillus of diphtheria, either following recovery from diphtheria or without himself having contracted the disease. A person who still harbors the bacilli as a result of a recent diphtheria infection shall be regarded as a case of the disease, and not as a carrier, until at least five weeks have elapsed after the date of the first release culture. After that time, the Health Officer may, at his discretion, regard such a person as a carrier rather than a case.

RULE 2. The local Health Officer upon the discovery of the carrier condition shall immediately advise the carrier or his guardians of the condition and give him detailed instructions regarding the precautions to be observed in the disposal of the secretions of the nose and mouth and in his association with other persons. If the carrier is a child attending school, the Health Officer shall immediately notify the medical school inspector, superintendent, or principal of the school, who shall immediately exclude him from the school.

RULE 3. A diphtheria carrier shall not leave the premises upon which he resides except under permission from the Health Officer, who shall issue such permission only for urgent reasons and when he is assured that necessary precautions will be taken for the protection of others. But no diphtheria carrier may be granted permission to attend church, Sunday School, moving picture shows, or other places of public assemblage; and he may be permitted to attend school only, when, because of the existence of numerous carriers following an outbreak of diphtheria, classes are conducted in separate rooms and the children who are carriers are prevented from mingling with other children.

RULE 4. Without permission from the Health Officer the premises occupied by a diphtheria carrier shall not be visited by children not residing there. When on such premises there are children other than the carrier, who are attending school or Sunday School, the Health Officer shall immediately have cultures taken from their noses and throats for examination; and when any such children are discovered to be free of diphtheria bacilli, they are to be kept apart from the carrier and not permitted to use the same eating utensils, toilet articles, etc., used by the carrier. Pending the report upon the cultures, all such children shall be excluded from school.

RULE 5. No diphtheria carrier shall engage in any occupation involving the handling of milk or other food to be consumed by others, except that, if a housewife, she may with the permission of the Health Officer continue to prepare food for the family or household, provided each member of the same has been shown, by means of the Schick test, to be immune to diphtheria. Should the carrier reside or be employed upon a farm producing milk for sale, the Health Officer may prohibit the sale of the milk, cream, butter, or cheese from such farm, except as provided in Reg. 37, Chapter II, of the Sanitary Code.

RULE 6. When a virulence test upon a culture from a diphtheria carrier has shown the organisms not to be virulent for guinea-pigs, the imposed restrictions may be removed by the Health Officer.

RULE 7. A diphtheria carrier may be regarded as free of the bacilli and be discharged from observation and restraint when two negative cultures, taken at intervals of no less than twenty-four hours, have been obtained.

RULE 8. Should a diphtheria carrier be unable or unwilling to observe the precautions herein indicated, the Health Officer may take such further action as may be necessary to safeguard public health, pursuant to Sections 25 and 326a of the Public Health Law.

NORTH CAROLINA.

No specific regulations regarding infection carriers, 1917.

OREGON.

Rules and regulations concerning the reporting and control of communicable diseases, 1918.

SECTION 11.—To prevent the possibilities of diphtheria carriers entering schools, cultures should be made from nose and throat of pupils before being admitted to school.

SECTION 20.—A constant lookout should be maintained for suspected typhoid carriers, and when found reported to the State Board of Health.

PENNSYLVANIA.

There are no specific regulations relating to the management of infection carriers. Each case is dealt with individually and controlled by virtue of the general powers granted by law to the Commissioner of Health.*

RHODE ISLAND.

No specific regulations regarding infection carriers.

SOUTH DAKOTA.

No specific regulations regarding infection carriers, 1915.

* As per letter from the Acting Commissioner of the Department of Health.

TENNESSEE.

No specific regulations regarding infection carriers.

TEXAS.

No specific regulations regarding infection carriers, 1917.

VERMONT.

(Reg. Board of Health, May 6, 1915.)

RULE 18.—*Carriers of Disease Germs.*—Any person who is a carrier of the disease germ of Asiatic cholera, diphtheria, epidemic dysentery, epidemic cerebrospinal meningitis, poliomyelitis (infantile paralysis), scarlet fever or typhoid fever shall be subject to such rules as the State Board of Health shall make for the control of such persons.

VIRGINIA.

No specific regulations regarding infection carriers, 1916.

WASHINGTON.

No specific regulations regarding infection carriers.

WEST VIRGINIA.

No specific regulations regarding infection carriers, 1916.

WISCONSIN.

*Rules of the State Board of Health Pertaining to the Prevention and Control of Communicable Diseases, 1917.**

Typhoid Fever.—In every case of typhoid the patient should be instructed of the danger he may be to the public and given instructions as to how to protect others against the infection which he is carrying. It is impossible to know whether a person is a carrier without a bacteriological examination of

* There are evidently no specific regulations, the above being notices to physicians.

his excreta, urine and feces. Therefore, in every case of convalescing typhoid, specimens of urine and feces should be collected in clean sterile bottles and sent to the laboratory together with a letter giving a full history of the patient. These patients should not be released from observation until two successive negative reports have been obtained.

Diphtheria.—A certain number of those who have diphtheria become carriers for a longer or shorter time. Sometimes the organisms persist in the throat for months after the patient is well. It is necessary, however, to keep these people isolated in order to prevent the spread of the disease.

There are a few who never had the disease but harbor the organism in their throats, which, when it finds its way into another's throat, will produce diphtheria. These carriers should be located so that the further spread of the disease may be prevented. The throat of every child entering school should be swabbed and the swab sent to the laboratory for diagnosis. Many school epidemics may be prevented by this means.

MUNICIPAL ORDINANCES, RULES AND REGULATIONS PERTAINING TO INFECTION CARRIERS.

ATLANTIC CITY, N. J.

No specific regulations.

BALTIMORE, MD.

No specific regulations.

BROCKTON, MASS.

No specific regulations.

CHICAGO, ILL.

Quarantine of Diphtheria Carriers.—Persons known to be diphtheria carriers must be placed in quarantine and isolated as far as possible. Children of the family who yield negative

cultures and who do not come in contact with the carrier in any way need not be excluded from the school. Quarantine of diphtheria carriers should be raised when two negative cultures from nose and throat of carrier are obtained on consecutive days.

COLUMBIA, S. C.

(Reg. Board of Health, October 19, 1915.)

1. That cultures shall be made from the secretions of the nose and throat of all other members of the family who have been in contact with the one suffering with diphtheria, in the event effective isolation of the patient is carried out, and that no one be allowed to go and come from the quarantined house unless said culture from the secretion of the nose and throat is negative for diphtheria bacilli.

2. That upon the termination of the case the school children of the family shall not be allowed to return to school until one culture from the secretion of the nose and throat is negative for diphtheria bacilli.

3. The health officer is enjoined to see that this regulation is carried out.

DETROIT, MICH.

Code of Regulations.—SECTION D.—Persons who have recently come in contact with persons suffering from cerebro-spinal meningitis, cholera, diphtheria, dysentery, erysipelas, paratyphoid fever, plague, lobar pneumonia, poliomyelitis, septic sore-throat, typhoid fever (and other communicable diseases) shall be subject to the rules of quarantine, isolation, etc., as are hereinafter provided for each specific disease.

GALVESTON, TEX.

No specific regulations.

MACON, GA.

No specific regulations.

MINNEAPOLIS, MINN.

The law under which the health department was organized gives the health officer the right to take reasonable precautions to protect the public. In the course of time customary proceedings have been established without the formality of legalizing them.

In typhoid fever members of the household are not allowed to work in foodstuffs until they are immunized (!?). Food-workers having had typhoid fever are not allowed to go back to work until a proper stool test has been made.*

NEW ORLEANS, LA.

No specific regulations.

NEWPORT NEWS, VA.

(Reg. Board of Health, March 5, 1915.)

18. The minimum period of quarantine for cases of diphtheria shall be fourteen days, except where two successive negative cultures are made on two successive days, and then the minimum period shall be seven days, provided that anti-toxin has been used (!?).

NEWTON, MASS.

No specific regulations.

"In cases where a person is found to be a carrier through a laboratory examination he is treated as a person ill with the disease in question and becomes amenable to the regular rules governing such disease."†

NEW YORK CITY.

(Reg. Department of Health, March 30, 1915.)

Infection Carriers.—SECTION 86.

REG. 3.—Any person who is a carrier of the disease germs of Asiatic cholera, bacillary dysentery, epidemic cerebro-

* As per letter from the Health Commissioner.

† As per letter from the Chairman of the Board of Health.

spinal meningitis, poliomyelitis or typhoid fever shall be subject to the regulations governing clinical cases of these respective diseases.

Examination of Specimens of Feces and Urine of Convalescent Patients.

(Reg. Department of Health, December 21, 1915.)

REG. 5.—In every case of typhoid fever the attending physician shall submit to the department of health specimens of feces and urine for examination for the presence of typhoid bacilli. Such specimens shall be submitted at least ten days after the patient's temperature reaches normal and before he or she shall resume his or her occupation. If in any case typhoid bacilli are found to be present in the excreta, such convalescent patient shall not resume his or her occupation without the permission of the department of health.

PHILADELPHIA, PA.

No specific regulations.

PORTLAND, ME.

(Reg. Board of Health, September 3, 1915.)

SECTION 1.—All persons quarantined for diphtheria and all contacts or exposed individuals of school age shall be removed from quarantine only after the obtaining of two successive negative throat cultures. The first culture shall be taken not earlier than the fourteenth day from the beginning of the quarantine and the second culture not earlier than twenty-four hours after.

SECTION 2.—In the case of a child of school age removed from an infected household at the beginning of quarantine, two throat cultures at least twenty-four hours apart shall be obtained as soon as possible, and if the cultures are negative such child may return to school at the end of one week's time after removal from infected household.

SECTION 3.—These rules have no bearing on the question of immunization, which should be performed as usual.

SALEM, MASS.

No specific regulations.

ST. LOUIS, MO.

No specific regulations.

MARITIME QUARANTINE AT NEW YORK.

Vessels Liable to Quarantine (Reg. Department of Health, December 21, 1915.)

Resolved, That section 352 of the Sanitary Code of the Board of Health of the Department of Health of the City of New York be and the same is hereby amended and made to read as follows:

SECTION 352.—*Vessels from Infected Ports, or Liable to Quarantine; Not to Be Brought Within 300 Yards of Docks or Piers Unless Permitted.*—No master, charterer, consignee, or other person shall order, bring, or allow (having power and authority to prevent) any vessel or person, or article therefrom, from any infected port, or any vessel, or person or article therefrom, liable to quarantine, according to the ninth section of the three hundred and fifty-eighth chapter of the laws of 1863 (or under any other laws, and whether such quarantine has been made or suffered or not), to come or be brought to any point nearer than 300 yards from any dock, pier, or building, in the city of New York without a permit therefor issued by the board of health, or otherwise than in accordance with the terms of said permit and with the regulations of said board. Nor shall any vessel, or person or thing therein or therefrom, having been in quarantine, come or be brought or be permitted to remain within the last-named distance of any last-named place, without a permit therefor issued by the board of health or otherwise than in accordance with the terms of said permit and with the regulations of said board.

QUARANTINE LAWS OF THE UNITED STATES.

An Act to Prevent the Introduction of Contagious Diseases from One State to Another or for the Punishment of Certain Offenses.

(U. S. Statutes at Large, Vol. xxvi, Chapter 51, p. 31.
Approved March 27, 1890.)

Be it Enacted by the Senate and House of Representatives of the United States of America in Congress Assembled, That whenever it shall be made to appear to the satisfaction of the President that cholera, yellow fever, smallpox, or plague exists in any State or Territory, or in the District of Columbia, and that there is danger of the spread of such disease into other States, Territories, or the District of Columbia, he is hereby authorized to cause the Secretary of the Treasury to promulgate such rules and regulations as in his judgment may be necessary to prevent the spread of such disease from one State or Territory into another, or from any State or Territory into the District of Columbia, or from the District of Columbia into any State or Territory, and to employ such inspectors and other persons as may be necessary to execute such regulations to prevent the spread of such disease. The said rules and regulations shall be prepared by the Supervising Surgeon-General of the Marine Hospital Service under the direction of the Secretary of the Treasury. And any person who shall willfully violate any rule or regulation so made and promulgated shall be deemed guilty of a misdemeanor, and upon conviction shall be punished by a fine of not more than five hundred dollars, or imprisonment for not more than two years, or both, in the discretion of the court.

An Act Granting Additional Quarantine Powers and Imposing Additional Duties upon the Marine Hospital Service.

(U. S. Statutes at Large, Vol. xxvii, Chapter 114, p. 449,
Approved February 15, 1893.)

SECTION 3.—That the Supervising Surgeon-General of the Marine Hospital Service shall, immediately after this

act takes effect, examine the quarantine regulations of all State and municipal boards of health, and shall, under the direction of the Secretary of the Treasury, coöperate with and aid State and municipal boards of health in the execution and enforcement of the rules and regulations of such boards and in the execution and enforcement of the rules and regulations made by the Secretary of the Treasury to prevent the introduction of contagious or infectious diseases into the United States from foreign countries, and into one State or Territory or the District of Columbia from another State or Territory or the District of Columbia; and all rules and regulations made by the Secretary of the Treasury shall operate uniformly and in no manner discriminate against any port or place; and at such ports and places within the United States as have no quarantine regulations under State or municipal authority, where such regulations are, in the opinion of the Secretary of the Treasury, necessary to prevent the introduction of contagious or infectious diseases into the United States from foreign countries, or into one State or Territory or the District of Columbia from another State or Territory or the District of Columbia, and at such ports and places within the United States where quarantine regulations exist under the authority of the State or municipality which, in the opinion of the Secretary of the Treasury, are not sufficient to prevent the introduction of such diseases into the United States, or into one State or Territory or the District of Columbia from another State or Territory or the District of Columbia, the Secretary of the Treasury shall, if in his judgment it is necessary and proper, make such additional rules and regulations as are necessary to prevent the introduction of such diseases into the United States from foreign countries, or into one State or Territory or the District of Columbia from another State or Territory or the District of Columbia, and when such rules and regulations have been made they shall be promulgated by the Secretary of the Treasury, and enforced by the sanitary authorities of the States and municipalities, where the State and municipal health authorities will undertake to execute and enforce them; but if the State or municipal

authorities shall fail or refuse to enforce said rules and regulations the President shall execute and enforce the same and adopt such measures as in his judgment shall be necessary to prevent the introduction or spread of such diseases, and may detail or appoint officers for that purpose. The Secretary of the Treasury shall make such rules and regulations as are necessary to be observed by vessels at the port of departure and on the voyage, where such vessels sail from any foreign port or place to any port or place in the United States, to secure the best sanitary condition of such vessel, her cargo, passengers and crew, which shall be published and communicated to and enforced by the consular officers of the United States. None of the penalties herein imposed shall attach to any vessel or owner or officer thereof until a copy of this act, with the rules and regulations made in pursuance thereof, has been posted up in the office of the consul or other consular officer of the United States for ten days in the port from which said vessel sailed; and the certificate of such consul or consular officer over his official signature shall be competent evidence of such posting in any court of the United States.

SECTION 5.—That the Secretary of the Treasury shall from time to time issue to the consular officers of the United States and to the medical officers serving at any foreign port, and otherwise make publicly known, the rules and regulations made by him, to be used and complied with by vessels in foreign ports, for securing the best sanitary conditions of such vessels, their cargoes, passengers and crew, before their departure for any port in the United States and in the course of the voyage, and all such other rules and regulations as shall be observed in the inspection of the same on the arrival thereof at any quarantine station at the port of destination, and for the disinfection and isolation of the same, and the treatment of cargo and persons on board, so as to prevent the introduction of cholera, yellow fever, or other contagious or infectious diseases; and it shall not be lawful for any vessel to enter said port to discharge its cargo or land its passengers except upon a certificate of the health officer at such quarantine station certifying that said rules and regulations have

in all respects been observed and complied with, as well on his part as on the part of the said vessel and its master, in respect to the same and to its cargo, passengers and crew; and the master of every such vessel shall produce and deliver to the collector of customs at said port of entry, together with the other papers of the vessel, the said bills of health required to be obtained at the port of departure and the certificate herein required to be obtained from the health officer at the port of entry, and that the bills of health herein prescribed shall be considered as part of the ship's papers, and when duly certified to by the proper consular or other officer of the United States, over his official signature and seal, shall be accepted as evidence of the statements therein contained in any court of the United States.

SECTION 7. That whenever it shall be shown to the satisfaction of the President that by reason of the existence of cholera or other infectious or contagious diseases in a foreign country there is serious danger of the introduction of the same into the United States, and that notwithstanding the quarantine defense this danger is so increased by the introduction of persons or property from such country that a suspension of the right to introduce the same is demanded in the interest of the public health, the President shall have power to prohibit, in whole or in part, the introduction of persons and property from such countries or places as he shall designate and for such period of time as he may deem necessary.

SECTION 8. That whenever the proper authorities of a State shall surrender to the United States the use of the buildings and disinfecting apparatus at a State quarantine station the Secretary of the Treasury shall be authorized to receive them and to pay a reasonable compensation to the State for their use, if, in his opinion, they are necessary to the United States.

INTERSTATE QUARANTINE REGULATIONS.

SECTION 27.—Common carriers shall not receive upon any car, vessel, vehicle, or conveyance operating in interstate

traffic any person affected with diphtheria, measles, or whooping-cough, or any person known to be a carrier of the bacillus diphtheriæ, unless removal and entrance permits have been granted by the State or local health officers at the places of departure and arrival, and unless said person is placed in a separate compartment and is accompanied by a properly qualified nurse or attendant and unless such nurse or attendant has pledged himself or herself in writing, to the common carrier, to comply with the following regulations while in transit:

(a) 1. Communication with the compartment within which the patient is traveling shall be restricted to the minimum consistent with the proper care and safety of the patient.

2. All dishes or utensils used by the patient en route shall be placed in a 5 per cent. solution of carbolic acid or disinfecting fluid of equivalent disinfecting value for at least one hour before being allowed to leave the compartment.

3. All sputum and nasal discharges from the patient shall be received in gauze or paper, which shall be deposited into a closed container and which shall be destroyed by burning or received in a 5 per cent. solution of carbolic acid or disinfecting fluid of equivalent disinfecting value placed in a covered vessel and allowed to stand undisturbed for at least two hours after the last addition thereto.

(b) Immediately upon the disembarkation of the patient the common carrier shall close the compartment the patient has vacated, without the removal of any of its contents, and shall keep the same closed until disinfection.

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